



ANNUAL REPORT
2016/17

FRAUNHOFER INSTITUTE FOR TOXICOLOGY AND EXPERIMENTAL MEDICINE ITEM

PERFORMANCE AND RESULTS

**ANNUAL REPORT
2016/17**

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FOREWORD

Dear Reader,

For Fraunhofer ITEM the year 2016 was a special year, not only because of its 35th anniversary. The institute was founded in Hannover as "Fraunhofer Institute for Toxicology and Aerosol Research ITA" in 1981 by aerosol physicist Prof. Werner Stöber and pathologist Prof. Ulrich Mohr, the latter an internationally renowned expert in the field of histopathological diagnosis in the respiratory tract of experimental animals. Some disciples of the founding fathers are still working at Fraunhofer ITEM and it is their merit that the institute has such outstanding expertise in the generation and analysis of aerosols and of their histopathologically visible toxicity upon inhalation. Today, 35 years later, the founders' concept of setting up a research institute with expertise in inhalation toxicology continues to be highly relevant. The change in the institute's management in 1996 and the following years were characterized in particular by the setup of a clinical research unit dedicated to experimental and clinical respiratory research and by a stronger focus being placed on the research-intensive interface between in-vitro, ex-vivo and in-vivo animal models on the one hand and the human target organism on the other hand. As a result, the scope of services and expertise offered by Fraunhofer ITEM was enhanced from translational toxicology for drugs and chemicals to include also translational medical research and clinical drug development, supported by an in-house proof-of-concept center. These clinical research and development capacities were combined with a pharmaceutical biotechnology department, set up and enhanced to include a GMP plant for process development and manufacturing of investigational biopharmaceuticals, and with the institute's expertise in inhalation toxicology including a corresponding technology platform, making Fraunhofer ITEM a unique institution in the publicly funded research landscape in Germany and Europe. This

enhanced expertise inevitably led to a change in the institute's name from ITA to ITEM: Fraunhofer Institute for Toxicology and Experimental Medicine. As another step in Fraunhofer ITEM's medical translational research, the new Division of Translational Biomedical Engineering and a corresponding Fraunhofer High-Performance Center with concurrent professorship at the Hannover Medical School were set up in 2016.

The end of the year 2016 was marked by a change in the institute's management. Twenty years after the previous appointment of an institute director, my colleague Prof. Dr. med. Norbert Krug is now taking over as executive director. Prof. Krug played a pivotal role in setting up the institute's clinical research department and the CRC Hannover. After my retirement at the end of March 2017, my position will finally be posted.

Let me take this opportunity to cordially thank all colleagues, friends and clients for many years of fruitful cooperation on the scientific and professional levels and often also in friendship. I hope you enjoyed this as much as I did. Please remain well-disposed towards Fraunhofer ITEM, its staff, and my successors – you will benefit from it.

Yours sincerely,



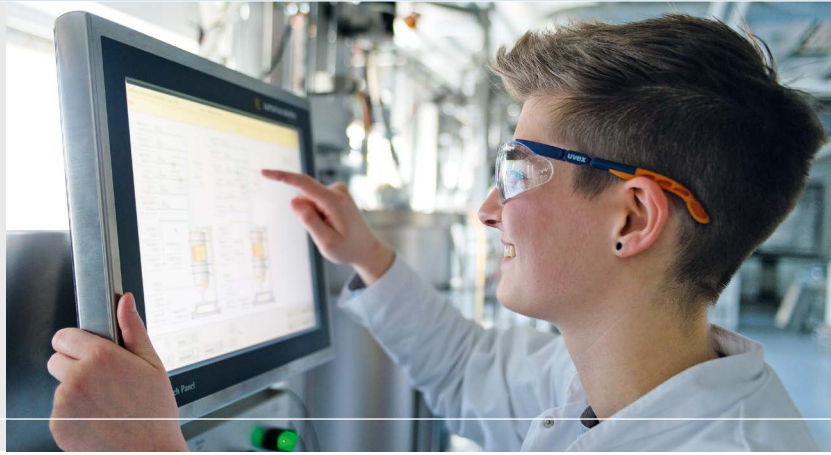
Uwe Heinrich



PROFILE OF THE INSTITUTE

Research at Fraunhofer ITEM is focused on human health – and this has been so for over 35 years. The emphasis is on two aspects: firstly, on protecting health from potentially harmful, in particular airborne substances, be they gases, aerosols, particles, fibers, or nanomaterials, and secondly, on investigating and developing diagnostic and therapeutic approaches in the field of inflammatory and allergic respiratory conditions, both at the preclinical and clinical levels. The lung and the airways are at the focus of research and development, but Fraunhofer ITEM is also investigating other subject areas. Examples are the development and manufacturing of biopharmaceuticals, tumor therapy, and translational biomedical engineering.





Protecting human health

Health protection includes environmental, occupational, and consumer protection. Fraunhofer ITEM supports industry and public authorities in the early identification and prevention of health hazards from new products and processes and thereby also promotes sustainable development of Germany as a business location.

In this context, Fraunhofer ITEM scientists investigate novel products and processes whose potential health hazards are as yet unknown, such as different nanomaterials. They evaluate the human exposure situation and develop suggestions on how to reduce or eliminate these potential hazards. For the experimental part of risk assessment, Fraunhofer ITEM has at its disposal the necessary know-how and toxicological test methods, in particular in the field of inhalation toxicology. For the required tests, complex atmospheres and test aerosols can be generated at laboratory scale and exposure scenarios can be reproduced for in-vitro or in-vivo studies. Special computerized mathematical exposure models are also developed and used for this purpose.

The scientists perform exposure and risk assessment on behalf of clients, based on their own experimental studies, literature searches, and data provided by the client. They prepare reports on test substances and support clients in the registration of chemicals and complex mixtures and in the assessment of substances falling under the European chemicals regulation REACH.

Preclinical research and development

With regard to inflammatory and allergic diseases of the respiratory tract Fraunhofer ITEM offers research and development services: from the molecular level to clinical trials. Methods of cell biology and molecular biology are used to validate novel target structures for diagnosis and therapy and optimize these during early development stages. Once possible drug

candidates have been identified, efficacy and safety tests are performed. Toxicological and safety pharmacological testing for drug registration is performed in compliance with GLP.

The institute offers a broad range of efficacy and drug safety studies and makes use of a variety of in-vitro test systems and models of inflammation, asthma, and lung infection. Using a tiered approach, the scientists first perform studies in cell culture models and subsequently gain further insights in complex tissue cultures and eventually in animal models. The use of human tissue in particular allows them to obtain human data at an early stage already, data of pivotal importance above all in the testing of biopharmaceuticals.

Throughout the entire research and development process, Fraunhofer ITEM scientists are keeping an eye on the ethical principle of the "3 Rs" – they are well aware of their great responsibility for the well-being of the animals they use in their experiments. The three Rs stand for Replacement – the use of alternative methods that avoid or replace the use of animals –, Reduction – strategies that will result in fewer animals being used – and Refinement – modification of husbandry or experimental procedures to minimize pain and distress. Research at Fraunhofer ITEM is geared to using less animals to answer research questions, to consistently improving research methods, and to replacing animal experiments by alternative methods whenever possible.

Biopharmaceutical manufacturing: from cell line to investigational medicinal product

A team of scientists, engineers and technicians in the institute's facilities in Braunschweig advises and assists clients and co-operation partners in the development of novel biopharmaceutical agents – from the development of recombinant production cell lines via the manufacturing of master and working cell banks, bioprocess development and scale-up, to the manufacturing of pilot batches of the novel biopharmaceutical



agent and sterile fill and finish of investigational medicinal products in the form of infusion solutions or in vials or ampoules (in compliance with GMP guidelines).

Early-phase clinical trials in the CRC Hannover

Efficacy and tolerability testing of novel drugs in humans is the critical step in medical translational research. The Clinical Research Center Hannover (CRC Hannover) offers optimal conditions for performing this step: state-of-the-art infrastructure including a total of 50 beds, 30 of which allow intensive monitoring of study participants. Fraunhofer ITEM has specialized in conducting clinical trials for the registration of pharmaceuticals for the therapeutic areas of allergy, asthma, COPD, and pulmonary fibrosis. The focus is on proof-of-concept studies in compliance with GCP guidelines, managed by highly qualified physicians. An in-house GMP laboratory enables production of intravenous dosage forms of IMPs.

With the Fraunhofer Challenge Chambers, special facilities for controlled challenge are available. They are among very few of this kind worldwide. In these chambers, pollen, house dust mite and other allergens, and also ozone can be dispersed in the air in a precisely controlled manner. The efficacy of novel medications to treat seasonal allergic rhinitis, for example, can be tested there under controlled allergen challenge conditions. And in challenge studies with LPS or ozone, the clinical efficacy of new anti-inflammatory drugs can be verified. The temporary inflammation of the airways in healthy study participants induced by short-term controlled ozone inhalation challenge resembles the inflammatory condition seen in COPD patients.

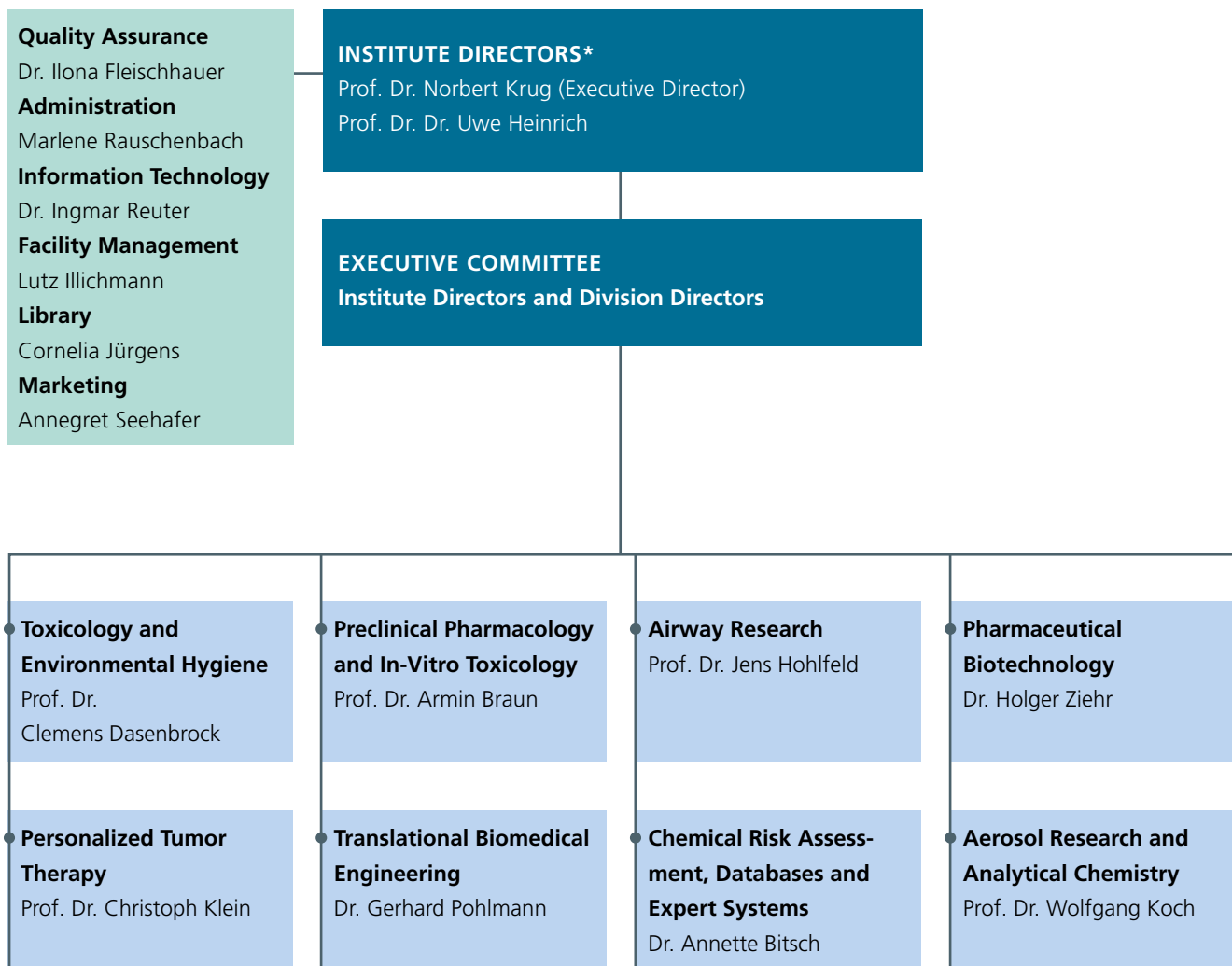
An essential prerequisite for the setup, further development, and operation of the Fraunhofer Challenge Chambers is the comprehensive expertise and many years of experience of the institute's aerosol technologists.

Translational Biomedical Engineering

Many years of experience of the institute's aerosol technologists, in particular their know-how on the aerosolization of substances and on the deposition and kinetics of inhaled materials have led to the Department of Medical Inhalation Technology being set up in 2015. At the end of 2016, this eventually resulted in the new Division of Translational Biomedical Engineering and corresponding business unit. Focuses of this division are on conducting and assisting the development of novel technologies for administration of medicinal aerosols on the one hand, and on conducting and assisting the development of active implants on the other hand.

In spring 2017, the new High-Performance Center Translational Biomedical Engineering was inaugurated, aimed at bringing medical devices from the lab into phase I of clinical development. It offers support in particular to small and medium-sized enterprises and to research institutions, given that dedicated manufacturing processes for medical devices and also regulatory requirements such as the new EU-wide Medical Device Regulation represent substantial economic hurdles for them. Collaborators in this new High-Performance Center include the Hannover Medical School, Laser Zentrum Hannover, Leibniz Universität Hannover, and in particular the two clusters of excellence REBIRTH and "Hearing4all" (in Hannover), besides research consortia such as "Biofabrication for NIFE", and Fraunhofer ITEM. The Center is funded by the Lower Saxony government and the Fraunhofer-Gesellschaft.

ORGANIZATIONAL STRUCTURE



* Prof. Uwe Heinrich was Executive Director until December 2016; Prof. Norbert Krug took over as Executive Director in January 2017.

as at January 2017

After 21 years of successful leadership, Prof. Uwe Heinrich ceded his position as Fraunhofer ITEM Executive Director to Prof. Norbert Krug on January 1, 2017.

Headed by the Institute Director(s) and the Executive Committee, Fraunhofer ITEM is organized in eight divisions. Two of these – “Translational Biomedical Engineering” and “Personalized Tumor Therapy” – were instituted at the beginning of 2017.

The Fraunhofer ITEM headquarters are in Hannover, the institute’s Division of Pharmaceutical Biotechnology has its facilities in Braunschweig on the campus of the Helmholtz Center for Infection Research, and the Division of Personalized Tumor Therapy is based in Regensburg’s BioPark.

GXP – QUALITY ASSURANCE ACCORDING TO INTERNATIONAL STANDARDS

Fraunhofer ITEM is striving to meet high quality standards with the services and products offered and to ensure maximum safety for trial subjects in clinical studies performed at the institute. Not only are the relevant legal regulations strictly complied with, but state-of-the-art regulatory requirements are invariably taken into consideration. To guarantee that the work performed at Fraunhofer ITEM satisfies internationally accepted quality standards, Fraunhofer ITEM has implemented the GXP quality assurance systems. These include Good Laboratory Practice (GLP), Good Clinical Practice (GCP), and Good Manufacturing Practice (GMP). With their respective scopes of application, these quality assurance systems cover the translational approach in the institute's spectrum of activities. The central service unit "Quality Assurance" is responsible for putting into practice the relevant quality assurance programs.

GLP compliance of non-clinical safety studies

To ensure reliability and traceability of the data generated in non-clinical health and environmental safety studies, the GLP principles include, among others, the following requirements:

- Clear assignment of responsibilities within the test facility
- Meticulous planning and qualified performance of every study
- Complete documentation of all procedures and preparation of comprehensive reports

By means of study-based and facility-based inspections, the service unit "Quality Assurance" continuously monitors compliance with these principles in the institute's departments that are concerned with toxicology, safety pharmacology, and analytics. For more than two decades, the competent authorities have performed regular inspections and have certified the institute's GLP compliance for a broad range of studies. The established quality assurance system thus guarantees to all sponsors an internationally recognized quality standard in the institute's non-clinical departments.

GCP standard of clinical trials

The ethical principles for biomedical research laid down in the Declaration of Helsinki form the basis of the GCP principles describing the quality standards to be met in clinical trials. At Fraunhofer ITEM, a broad range of measures ensures that these requirements are met in trials falling under the German Drug Act and performed on behalf of international sponsors and also in clinical research projects. The service unit "Quality Assurance" assists the clinical investigators in fulfilling their responsibilities by closely monitoring implementation of the quality-relevant processes under aspects of GCP and by routinely checking the corresponding documentation. The institute's sponsors have rated the quality level reached as GCP-compliant.

In the Clinical Research Center Hannover (CRC Hannover), cooperated as a Fraunhofer research institution by Fraunhofer ITEM, the Hannover Medical School (MHH) and the Helmholtz Center for Infection Research (HZI), the service unit "Quality Assurance" performs cross-project and coordinating tasks in the field of quality assurance, thereby maintaining a high level of uniform quality standards in the CRC Hannover facilities. The synergies resulting from the scientific cooperation of the partners in the



CRC Hannover thus go hand in hand with guaranteed maximum protection of all trial subjects and fulfillment of sponsors' quality requirements.

GMP quality standard

The Division of Pharmaceutical Biotechnology in Braunschweig has comprehensive expertise and a long track record in the development of GMP manufacturing processes for biopharmaceuticals. For this purpose, the division has established a GMP quality assurance system to ensure compliance with the German Drug Act, the German Ordinance on the Manufacturing of Medicinal Products and Active Ingredients (AMWHV), and the European Union GMP Guide. Other guidelines are also taken into account, e.g. those of the ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use).

The division is operating clean rooms of grades D to B according to Annex 1 of the EU GMP Guide, subdivided into different zones satisfying the respective hygiene and pressure requirements, and using steam and water in the qualities prescribed by the European Pharmacopoeia. All critical equipment for the manufacture of medicinal products has been qualified in compliance with Annex 15 of the EU GMP Guide. An automated filling machine enclosed in a restricted-access barrier system (RABS) of clean-room grade A is available for manufacturing of small batches of sterile investigational medicinal products (IMPs) for use, for example, in clinical trials or stability tests.

The division has been inspected on numerous occasions by the competent authorities and has been granted a manufacturing license for active biopharmaceutical ingredients and investigational medicinal products.

Biopharmaceutical products can thus be developed jointly with small biotech start-ups and academic partners, and can consistently be manufactured to the required quality – from the cell line to the released IMP.



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STAFF AND INSTITUTE BUDGET PERFORMANCE

At the end of 2016, Fraunhofer ITEM staff amounted to 303 persons:
 8 apprentices
 40 students (including Ph.D. students)
 255 scientific, technical, and administrative staff

In 2016, the institute's budget reached a level of 26.4 million euros. Financing by acquired funding amounted to 72 percent. The share of industrial income in the institute's budget was 45 percent. Investments of Fraunhofer ITEM amounted to approximately 1.3 million euros.

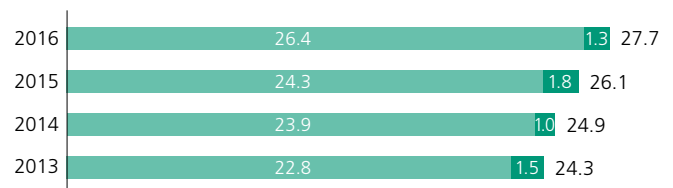
Fraunhofer ITEM staff

Number of employees



Fraunhofer ITEM total budget

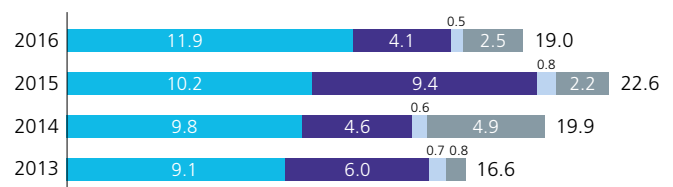
In million euros



■ Operating budget
 ■ Investments

Fraunhofer ITEM sponsors and external income

In million euros



■ Industry and commercial associations
 ■ Public sector
 ■ EU
 ■ Other

BOARD OF TRUSTEES

The boards of trustees of the individual Fraunhofer Institutes act as purely advisory bodies to their institute's management. The members come from academia, industry, and government agencies. In 2016, the Fraunhofer ITEM board or trustees was made up of the following members:

Dr. Eckhard von Keutz

Chairman of the board or trustees
Senior Vice President, Global Head Early Development,
Bayer HealthCare AG

Prof. Dr. Christopher Baum

Deputy Chairman of the board or trustees
President and member of the Presidential Council
responsible for the Division of Research and Teaching of the
Hannover Medical School

Dr. Marcus Beiner

Deputy Head of the Department Research and Innovation,
Head of the Division of Life Sciences, Humanities,
Social Sciences, and Sustainable Development,
Lower Saxony Ministry of Science and Culture

Prof. Dr. Dieter Bitter-Suermann

Former President and member of the Presidential Council
responsible for the Division of Research and Teaching of the
Hannover Medical School

Prof. Dr. Ulrich Deschl

Head of Nonclinical Drug Safety,
Boehringer Ingelheim Pharma GmbH & Co. KG

Prof. Dr. Paul-Georg Germann

Head Preclinical Safety Germany, AbbVie Deutschland GmbH

Prof. Dr. Thomas Jung

Executive Director, Jung & Partners GmbH, Switzerland

Dr. Günther Karmann

Executive Director, Karmann Consulting GmbH

Prof. Dr. Hillel S. Koren

Managing Director, Environmental Health, LLC;
former Director Human Studies Division,
United States Environmental Protection Agency;
Research Professor Carolina Environmental Program,
University of Carolina at Chapel Hill, USA

Dr. Edgar Leibold

Vice President Product Stewardship, BASF SE

Prof. Prof. h. c. Dr. med. Thomas Lenarz

Professor and Chairman of the Department of
Otorhinolaryngology, and Director of Deutsches HörZentrum,
Hannover Medical School

Prof. Dr. Reinhard Pabst

Lower Saxony Professorship in Immunomorphology,
Hannover Medical School

Prof. Dr. Klaus F. Rabe

Medical Director and Executive Medical Officer,
LungenClinic Grosshansdorf;
Endowed Professorship in Internal Medicine/Pneumology,
Faculty of Medicine, Kiel University

Prof. Dr. Gerhard Schlüter

Consultant in toxicology;
former Global Head Toxicology, Bayer HealthCare AG

Dr. Thor A. Voigt

Medical Director Germany,
Boehringer Ingelheim Pharma GmbH & Co. KG

Dr. Torsten Wagner

Senior Vice President, Corporate Technical Operations,
Merz Pharma GmbH & Co. KGaA

CRC HANNOVER

State-of-the-art center for clinical research

The Clinical Research Center Hannover (CRC Hannover) is a center for early-phase clinical trials that is the only one of its kind in Germany, used collaboratively by three well-established research institutions: Hannover Medical School (MHH), Helmholtz Center for Infection Research (HZI), and Fraunhofer ITEM. As a proof-of-concept center it provides a platform for safety and efficacy testing of novel drugs, diagnostic methods and medical devices on their way to marketing authorization. In addition to proof-of-concept trials, HZI is conducting the “German National Cohort” study, the largest health study in Germany,

at the CRC Hannover. Over the next few years, 10,000 individuals will be examined and questioned here. The aim of the study is to provide information facilitating early detection, prevention, and treatment of wide-spread conditions such as cardiovascular and respiratory diseases, cancer, diabetes, dementia, infections, and diseases of the immune system. Since its inauguration in fall 2014, the CRC Hannover has become established as a leading-edge study center.

For the performance of phase-I studies (first-in-man trials with novel drugs to test their safety in a small number of volunteers) and phase-II studies (required to provide the proof of concept of novel medications or therapeutic approaches





in man), a total of 50 beds are available, 30 of which allow intensive monitoring of study participants. The technical equipment in the CRC Hannover enables comprehensive diagnostics, complemented by the additional infrastructure of the three cooperating research institutions.

The first-rate equipment available at the CRC Hannover allows the Fraunhofer scientists to do airway research at a high level. For example, they have at their disposal a cutting-edge MRI scanner with a xenon polarizer. This imaging technology allows them to visualize not only lung tissue, but also the air in the lungs and even the air passing into tissue. The establishment of this method represents a milestone, in particular for the search for biomarkers that are suitable to indicate whether lung tissue is healthy or diseased. Such diagnostic biomarkers in turn can then be used to develop new methods for drug testing.

The CRC Hannover furthermore hosts one of the most modern biobanks in Germany: the Hannover Unified Biobank (HUB) of the Hannover Medical School – a highly automated, state-of-the-art depository for biomaterials with affiliated preanalytics. This is a great benefit to the institutions cooperating in the CRC Hannover: it gives them the possibility to store biomaterials from patients required for medical research – under high quality standards. The HUB is one of only few biobanks in Germany that have been certified in accordance with DIN EN ISO 9001:2008.

The scientific activities of course are priority at the CRC Hannover. And yet, the representative building with its state-of-the-art technical equipment, spacious facilities and on-site catering service is used increasingly also as a conference center. The conference room with view into the greenery and a close-by terrace offers room for 120 participants. By coupling the conference room and the spacious foyer, a setting for 320 guests can be arranged. The CRC Hannover each year hosts, for

example, the Fraunhofer seminar “Models of Lung Disease”, organized by Fraunhofer ITEM in close cooperation with the German Center for Lung Research (DZL). This two-day event provides an international platform for intense discussions between industry, academia and authorities about predictive disease models and translational lung research, accompanied by poster presentations and an industry exhibition. Another example of the CRC Hannover being used as a conference center is the “Pulmonary Fibrosis” patient seminar, organized at regular intervals by BREATH, the Hannover DZL site. The TRAIN Academy professional education program “Translational Research & Medicine: From Idea to Product” is yet another series of lectures the CRC Hannover hosts at regular intervals, besides numerous other external and internal events.



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SELECTED NEWS

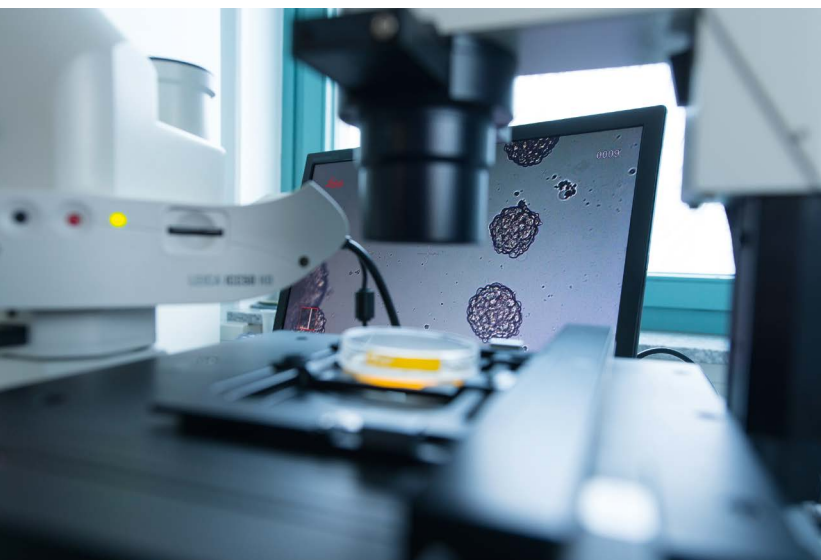
“Models of Lung Disease” – seminar series with tradition

The seminar series “Models of Lung Disease” has meanwhile become a tradition at Fraunhofer ITEM. In January 2016, international experts in translational lung research got together for the 15th time to exchange ideas and share information. The aim of this seminar was to discuss new developments in experimental lung research from industry and academia and compare different models and approaches. Different disease areas, including asthma, COPD, pulmonary fibrosis, and lung infection, were addressed in selected presentations covering different phases of research, from basic research via preclinical models to early-phase clinical trials. Participants were highly satisfied with the well-balanced mixture of interesting presentations, personal conversations, and guided tours.



New mechanisms of early metastatic spread in breast cancer discovered

The dogma that cancer cells seed mainly from advanced tumors seems no longer tenable. Scientists of the Regensburg-based Fraunhofer ITEM Division of Personalized Tumor Therapy, the University of Regensburg and the Icahn School of Medicine at Mount Sinai in New York have discovered new mechanisms of early metastatic spread in breast cancer. Results were published in the renowned journal “Nature” at the End of 2016. The scientists are hoping that these fundamentally new findings will advance cancer research substantially.



November of Science – open house day

With a versatile program for adults as well as for children, Fraunhofer ITEM and CRC Hannover opened their doors to the public for one day in November 2016 to give insight into the broad spectrum of research activities for human health. Numerous visitors enjoyed guided tours to laboratories and the clinical facilities, lectures on research topics of current interest, and short hands-on trainings for youngsters from 8 to 14 years of age. The “November of Science” is a project of the Initiative Science Hannover, in which eight Hannover-based universities and Fraunhofer ITEM have been participating since its beginning in 2007.



Prizes for scientific work

Research work done at Fraunhofer ITEM was honored at various conferences and congresses in 2016, for example, by poster prizes or the opportunity to present a subject matter in a plenary talk. Two junior scientists were awarded poster prizes during the Annual Meeting of the German Center for Lung Research: Sebastian Konzok for his poster titled “Bacterial and viral PAMPs and cellular DAMPs lead to activation of the inflammasome in human lung tissue ex-vivo” and Arne Gaida for his poster titled “A dual-center study to compare breath volatile organic compounds from smokers and non-smokers with and without COPD.” At the same

conference, the abstracts submitted by Helena Obernolte (disease area “Asthma & Allergy”) and Olaf Holz (disease area “COPD”) were selected for plenary presentations from among 230 submitted abstracts. Elaine Cabral Serrão was awarded a prize for her poster titled “A novel disruptive IgE inhibitor: efficacy assessment in non-human primate and human precision-cut lung slices” at the EAACI 2016 Congress. And at the ERS 2016 Congress, Christina Hesse’s abstract “Induction of pro-fibrotic biomarkers in precision-cut lung slices (PCLS)” won the award of “Best Abstract of Young Investigators”.

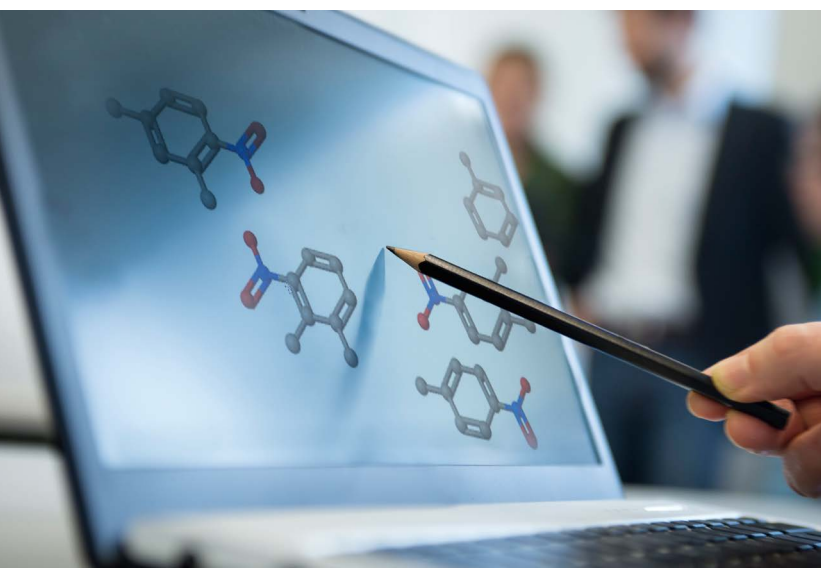
EU-ToxRisk

Fraunhofer ITEM is participating in the European research project "EU-ToxRisk" that was kicked off in January 2016. Its aim is to lay new foundations for a paradigm shift in toxicology – towards more efficient and animal-free hazard and risk assessment of chemicals. An international consortium of 39 partner organizations from academia, industry and regulatory authorities is participating in this project receiving funding of 30 million euros. Fraunhofer ITEM is bringing in its expertise with a focus on inhalation toxicology: from alternative methods for assessment of inhalation toxicity to the development of in-silico methods for use in regulatory contexts.



Workshop on in-vitro toxicology – focus on inhalation

The one-day workshop "Cell-based in-vitro methods for investigations on biological effects of inhalable compounds" in November 2016 gave scientists and consultants from academia and industry insights into the emerging field of in-vitro toxicology of inhalable substances. They learned about in-vitro methods as powerful and predictive methods enabling in-vitro investigation of the biological effects of airborne compounds in the sense of the 3Rs. Investigation of nearly all kinds of inhalable atmospheres, such as dry or droplet aerosols, sprays, emissions during use of consumer products, exhausts, and nanoparticles, is possible today using appropriate and relevant cell-based in-vitro methods.



High-Performance Center inaugurated

In spring 2017, the new High-Performance Center Translational Biomedical Engineering was inaugurated, aimed at bringing medical devices from the lab into phase I of clinical development and at helping in particular academic institutions and SMEs to overcome economic hurdles of the development process. The new Center is headed by Prof. Theodor Doll. Collaborators include the Hannover Medical School, Laser Zentrum Hannover, Leibniz Universität Hannover, and in particular the two clusters of excellence REBIRTH and "Hearing4all" (in Hannover), besides research consortia such as "Biofabrication for NIFE", and Fraunhofer ITEM. The Center is funded by the Lower Saxony government and the Fraunhofer-Gesellschaft.

The focus of the new Center is on technological solutions for inhaled drug delivery, commonly referred to as smart drug devices, and on active implants, i.e. electrical stimulation systems such as cochlear implants. The photograph shows Prof. Lenarz (sitting at the front), Chairman of the Department of Otorhinolaryngology of the Hannover Medical School, demonstrating on a model the insertion of such an implant into a patient's cochlea. His audience: Dr. Gabriele Heinen-Kljajić, Lower Saxony Minister of Science and Culture, Prof. Theodor Doll, Head of the High-Performance Center, Prof. Norbert Krug, Fraunhofer ITEM Director, Prof. Reimund Neugebauer, President of the Fraunhofer-Gesellschaft, and Prof. Christopher Baum, President of the Hannover Medical School (from left to right).



DRUG DEVELOPMENT

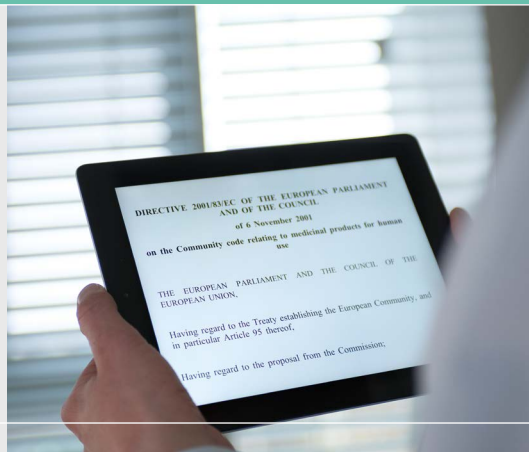


OUR SERVICES: FROM DRUG CANDIDATE TO PROOF OF CONCEPT

We are committed to translating innovative drug research into therapeutic applications – safely, reliably and efficiently. Based on our scientific expertise, we offer appropriate methods and approaches to this end. With custom-tailored development strategies, we support our clients in process development for and manufacturing of active biopharmaceutical ingredients and sterile investigational medicinal products, in preclinical testing – both pharmacology and toxicology – and in early-phase clinical trials from first-in-human to the clinical proof of concept.

Our state-of-the-art equipment and innovative research approaches allow us to develop new methods and techniques – also in cooperation with our clients. Already in the early phase of drug development, we provide assistance as independent consultants and negotiators in the dialog between applicant and regulatory authority. We work in compliance with regulatory and legal requirements for drug development and according to the quality assurance systems GLP, GMP, and GCP.

With the services offered by Fraunhofer ITEM, we can cover either the complete drug development chain or individual phases on the way from the drug candidate to clinical trials.



Development of novel biopharmaceuticals

A multidisciplinary team of biologists, chemists, pharmacists, engineers, and technicians assists our clients on their way from the idea for a new biotherapeutic via development of a production cell line to GMP manufacturing of the investigational medicinal product (IMP) released for use in clinical trials. This team guides you along the entire regulatory pathway to your approved IMP dossier. Our clients benefit from our profound knowledge accumulated over 20 years from a broad range of biopharmaceutical candidates – from simple proteins to complex structures such as viruses and cells. Our service portfolio includes:

- Biopharmaceutical, technical, and regulatory consultancy
- Development of mammalian and microbial production cell lines
- GMP manufacturing of master and working cell banks
- Development of complex upstream and downstream sequences with subsequent upscaling
- GMP manufacturing of API pilot charges
- Release testing of biopharmaceutical APIs and IMPs
- Sterile manufacturing and release of IMPs (liquid dosage forms)

Regulatory research and risk assessment in drug development

Fraunhofer ITEM has combined its expertise in drug research and development with its experience in registration and risk assessment of chemicals. With these forces joined, the institute is uniquely positioned to support clients in regulatory affairs in the drug development process. Our scientists explore, develop, and validate new approaches to manufacture, characterize, and test innovative medicinal products, ensure regulatory input on these approaches, and implement them in product development in cooperation with the client. Our service portfolio includes:

- Preparation of a regulatory strategy to take products from lab to market
- Interaction with regulatory authorities
- Preparation of the required documentation
- Risk assessment
- Regulatory research



Preclinical testing

For preclinical development of a drug candidate we offer a broad spectrum of disease-relevant and toxicological models. Our outstanding expertise, many years of experience with partners from the pharmaceutical and biotech industries, and state-of-the-art equipment provide the foundation for our scientific solutions and custom-tailored services. Our special focus is on inhalation toxicology and immunotoxicology.

For efficacy testing of drug candidates we offer disease-relevant models for all therapeutically relevant diseases of the respiratory tract such as COPD, asthma, pulmonary fibrosis, infections, and tumors. We are committed to enabling reliable prediction of the efficacy of drug candidates – by constant development of new methods in collaboration with academic institutions and research centers. For toxicology testing of drug candidates we offer the following services and expertise:

- In-vitro studies (genotoxicity, molecular toxicity, screening assays)
- Ex-vivo studies (e.g. precision-cut lung slices)
- In-vivo studies (relevant species, single-dose and repeated-dose toxicity, reproductive toxicity)
- Safety pharmacology (core battery)
- Testing strategies to accompany clients during scientific advice and registration processes
- Track record including biopharmaceuticals, oligonucleotide-based therapeutics, and ATMPs
- Study performance according to OECD GLP, where applicable

Clinical trials

Finding the most appropriate model for your proof of concept and the most suitable study design are challenges we can successfully handle with our excellent medical expertise and strong academic background. We support clients in the development of drugs targeting respiratory and allergic diseases and do patient-oriented research to help people suffering from these conditions. A broad range of challenge models is available for clinical studies on respiratory diseases such as asthma, allergic rhinitis, COPD, and interstitial lung diseases (idiopathic pulmonary fibrosis in particular). Our studies are performed by a highly qualified and dedicated team of physicians, study nurses, and medical documentation specialists, accompanied by an independent quality assurance unit. The following services and infrastructure are available:

- Fraunhofer Challenge Chambers: challenge chambers for proof-of-concept studies with sophisticated study designs, enabling exposure of test subjects to natural pollen, allergen extracts, or ozone
- Inhaled allergen challenge
- Segmental challenge during bronchoscopy
- Exercise testing (spirometry)
- Collection and analysis of human samples
- Biomarker analysis
- Imaging: non-invasive MRI techniques
- In-house GMP laboratory for production of intravenous dosage forms of IMPs
- Patient/volunteer database

PROJECTS

Research on human embryonic hematopoiesis in a teratoma model

In vertebrates, hematopoietic stem cells (HSCs) are located mainly in the bone marrow. In addition to their ability to self-renew, these cells continuously produce progenitor cells which mature into blood cells. Pathological alterations in the hematopoietic system often have very critical effects and in some cases the only treatment option is bone marrow transplantation. The availability of donors, however, is limited. This is why scientists have long been trying to synthesize HSCs artificially in cell culture systems from stem cells. Despite many decades of research, this goal has not been reached to date. A novel approach to studying the complex environment of functional HSCs is the use of teratoma formation as a model

of embryogenesis. Teratomas are germ cell tumors which can be induced by injection of pluripotent stem cells in immunodeficient mice. They include various cell types and progenitors. During teratoma formation, some cells develop into HSCs displaying the functional characteristics of natural HSCs. Within the scope of the REBIRTH cluster of excellence, scientists of the Hannover Medical School together with Fraunhofer ITEM scientists are using this model to investigate possibilities of supporting artificial production of HSCs. Gathered insights are planned to be transferred to cell culture methods, to get closer to the aim of successful de-novo generation of HSCs.



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Antibody-mediated neutralization of specific intestinal bacteria

The small and large intestines play an important role in the human immune system, hosting approximately 70 percent of all immune cells. The gut flora represents a key player in this context. Different immunological diseases such as allergies have been increasingly linked to an impaired intestinal immune system. In a project funded by the Fraunhofer research program "Discover", scientists of the Fraunhofer Institute for Cell Therapy and Immunology IZI in Leipzig have developed a specific antibody with the aim to neutralize certain gut bacteria. Together with scientists from Fraunhofer ITEM, they hypothesized that this would result in an alteration of the intestinal microbiome, thereby directly affecting the immune

system and thus modulating the immune response. In a first proof of concept, the aim was to achieve a reduction in disease symptoms and severity in a mouse model of allergic asthma after treatment with this antibody. Indeed, Fraunhofer ITEM scientists observed a substantial reduction of the allergic airway inflammation in the animals after oral antibody treatment. Such a correction of the microbiome, aimed at modulating the immune system, holds promising potential for the development of a novel pharmacotherapeutic approach to treat a whole range of allergic and autoimmune disorders.



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Precision-cut lung slices enable also research on pulmonary fibrosis.



Pulmonary fibrosis: ex-vivo model for research and drug testing

Pulmonary fibrosis is a rapidly progressing lung disease, incurable to date and usually fatal. Hallmarks of this medical condition include uncontrolled proliferation of fibroblasts and excessive production and deposition of extracellular matrix. These pathological changes eventually lead to alterations in lung architecture, causing irreversible dysfunction of the organ. Most insights into the underlying pathogenic mechanisms so far have been gained in in-vivo animal models. Although functional and biochemical features in these models closely resemble those found in patients, animal models often do not entirely reflect all features of the disease. Fraunhofer ITEM scientists are developing a novel ex-vivo approach, allowing

investigation of the human disease with higher translational relevance. By stimulating ex-vivo lung tissue slices with relevant pro-fibrotic mediators they were able to induce different biomarkers of fibrosis in non-fibrotic human lung tissue. This model can help to further elucidate the pathogenic mechanisms of pulmonary fibrosis; in addition, it can be used for preclinical testing of anti-fibrotic drug candidates. Already diseased tissue can also be evaluated, for example, to study the expression of pro-fibrotic markers or for pharmacological drug testing and preclinical development of new medications.



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Quantification of the local inflammation in the lung by MRI

The method of segmental lung challenge in humans by local bronchoscopic application of endotoxin was developed at Fraunhofer ITEM several years ago for efficacy testing of novel anti-inflammatory drugs. It includes determination of the inflammatory cell count in the lung lavage fluid collected during bronchoscopy to evaluate the degree of the inflammation. In an ongoing clinical trial, the endotoxin challenge model is used in healthy test subjects to provide the proof of principle for a novel anti-inflammatory drug to treat chronic obstructive pulmonary disease. For this purpose, a GMP process for importing endotoxin from an American supplier and labeling it for clinical trials was first established at Fraunhofer ITEM. To

quantify the degree of the local inflammation, the researchers are using a new method in parallel with the inflammatory cell count determined by bronchoscopy: magnetic resonance imaging (MRI). The aim is to quantify the degree of the local inflammation also noninvasively by means of this imaging method. The proof of concept for this method has already been provided for local allergen challenge (Vogel-Claussen et al., Am J Respir Crit Care Med, 2014; Renne et al., Radiology, 2015). A total of 50 test subjects will be included in this trial. Results are expected for mid-2017.



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Mobile patients instead of mobile challenge chambers

Allergen Challenge Chambers (ACCs) allow allergic test subjects to be challenged with constant pollen concentrations in drug trials to evaluate anti-allergic medications. Furthermore, ACCs tend to be used more and more to test formulations for specific immunotherapy (desensitization), as a natural pollen season with low pollen count may, in unfavorable cases, not be sufficient to demonstrate efficacy of an immunotherapy. Comprehensive immunotherapy studies, however, are often performed at many different centers simultaneously, sometimes even in different countries. This is why attempts have been made to reach all study participants in the involved study centers by means of mobile ACCs. Fraunhofer ITEM is pursuing a contrary approach with its Fraunhofer ACC: the ACC does not travel to patients, but patients travel to

the Fraunhofer ACC. Recently, another comprehensive immunotherapy trial based on this concept was successfully completed in the Fraunhofer ACC. In the course of this study, over 300 test subjects from three different countries – Germany, Poland, and Spain – traveled to Hannover before and after the treatment under evaluation, to undergo challenge with grass pollen in the Fraunhofer ACC. Language barriers were overcome by using interpreters. Feedback from patients was positive without exception, despite the long distances some of them had to overcome, and the study sponsor equally rated the study a success. The concept of “mobile patients” thus can continue to be used in future multinational trials.



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Production of therapeutic phages for efficacy and infection studies

Phages have been known for a long time to offer an efficient alternative to antibiotics. Despite only few side effects, however, they have not become firmly established in the Western market so far, due to the broad availability of antibiotics. The Division of Pharmaceutical Biotechnology has already built up expertise in GMP manufacturing of therapeutic bacteriophages. As a result of the ongoing public debate about increasing resistances to antibiotics and the search for alternatives motivated thereby, the demand for such expertise has been rekindled. In a first collaborative project with Leibniz Institute DSMZ (German Collection of Microorganisms and Cell Cultures GmbH), Fraunhofer ITEM scientists are developing manufacturing steps for the production of two *Acinetobacter baumannii* phages, geared to GMP quality requirements. The phages thus pro-

duced will be tested as anti-infective agents against *A. baumannii* in a murine infection model at Charité in Berlin. To this end, Fraunhofer ITEM scientists have collaborated with colleagues from Leibniz Institute DSMZ to develop cultivation strategies for *Acinetobacter* host strains and phages and establish suitable primary recovery techniques for preliminary treatment of the phage lysate. The next step will be to develop cost-efficient purification methods for the phage lysate, aimed at removing endotoxins from gram-negative *A. Baumannii* in particular as completely as possible. These activities will further enhance Fraunhofer ITEM's expertise in the production of therapeutic phages.



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Optimization of production cell lines by means of microRNA

Recombinant proteins for therapeutic use in humans are frequently manufactured by means of eukaryotic cell cultures. This is due to the complex glycosylation pattern of such therapeutic proteins. The manufacturing platforms used today for this purpose, consisting of cell lines of human or animal origin and plasmids with special expression cassettes, enable continued optimization. One option to improve cell growth, expression (i.e. productivity) or cell viability is the use of microRNA (miRNA). Via this type of RNA, which is naturally present in cells, biotechnologists can influence the expression of genes that are directly or indirectly involved in the expression of the product gene. The presence of certain miRNA sequences, for example, allows the number of ribosomes

in the cell to be increased. A potential limitation of the expression due to translation can thus be avoided. The miRNA can be stably integrated into the cell genome, so that it will be continuously expressed. Alternatively, it is also possible to integrate miRNA into the expression plasmid of the product and achieve its expression in the cell in this way. A choice of expression plasmids with different miRNA sequences can thus be generated, and an expression plasmid tailored to the expression of the specific product gene can then be selected in each case. At Fraunhofer ITEM in Braunschweig, miRNA sequences are an integral part of cell line development.



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Development of a robust CHO platform for protein production

The biopharmaceutical industry preferably uses animal cells, CHO cells in particular, for the manufacturing of therapeutic glycoproteins. The aim of this project is to develop in-house CHO production cell lines and corresponding bioprocesses for the manufacturing of biopharmaceutical glycoproteins. To establish this technology platform, it is planned to develop the expression of different monoclonal antibodies and highly glycosylated recombinant proteins by means of the in-house CHO suspension cell line. Glycoengineering and cell line engineering shall be used to improve product quality and quantity. This will enable improvements, for example, in cell viability,

product yield, or antibody efficacy (antibody-dependent cellular cytotoxicity, ADCC). Furthermore, preservation of a defined glycosylation pattern of the glycoproteins is becoming increasingly important for market authorization of biopharmaceuticals, given that glycoproteins are characterized more and more by means of their glycosylation pattern. Based on the research work performed to date, it is intended to develop a CHO cell-based technology platform that will guarantee cost and time-efficient production of a broad variety of glycoproteins still complying with all regulatory requirements.



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CHEMICAL SAFETY AND ASSESSMENT

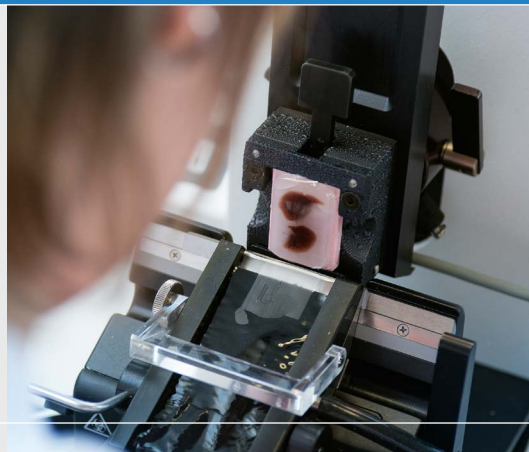


OUR SERVICES: FROM RISK ANALYSIS TOWARDS SAFE PRODUCTS

The general objective of chemical risk assessment methodologies is to facilitate both scientific and data-informed decision-making. The process of chemical risk assessment has both qualitative and quantitative components and is generally composed of four steps: hazard identification, dose-response assessment (i.e. DNEL derivation), exposure assessment, and risk characterization.

Our comprehensive experience at Fraunhofer ITEM covers investigation of chemicals, (nano)particles, fibers, and complex mixtures as they occur at workplaces, in the environment, and in consumer products. Based on our core competencies, we provide information supporting decision-makers in reducing potential risks and enabling safe use of chemical products.

The services offered by Fraunhofer ITEM assist you on the way from risk analysis towards safe products.



Development of test methods and analytical procedures

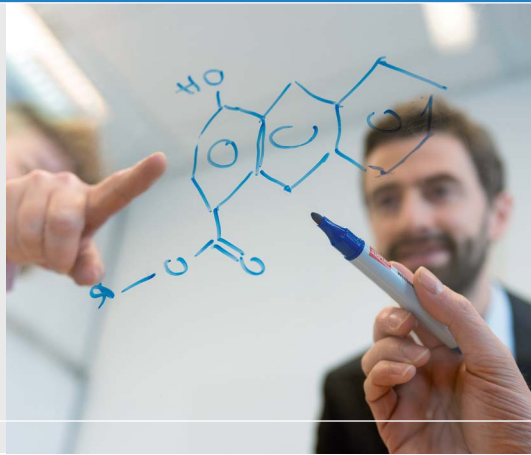
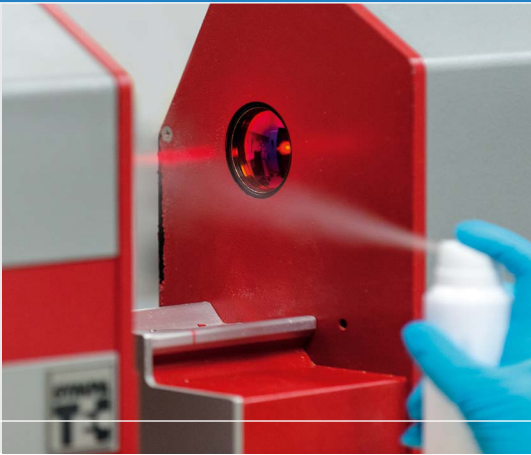
We offer our clients comprehensive consulting and expert opinions in analytical issues that are often beyond the scope of commercially available routine analyses. In close contact with our clients, we develop custom-tailored analytical strategies. For problem-solving that meets the client's specific requirements, we offer:

- Development of analytical methods and validation in compliance with the relevant guidelines
- Analytical studies (both GLP and non-GLP) required for registration and authorization
- Target and non-target analysis of inorganic and organic compounds (e.g. aldehydes/ketones, dyes, pharmaceuticals, BTX, PAHs, pesticides, VOCs, SVOCs, metals, and compounds typical of explosives)
- Characterization of complex mixtures in environmental samples and biological matrices
- Structural elucidation of drug substances and natural products and of their metabolites
- Protein mass spectrometry, structural elucidation of modified proteins, de-novo sequencing
- Metabolism research and accompanying analyses to investigate toxicokinetic endpoints
- Development of instruments and methods for measurement, collection, and generation of aerosols
- Development of methods and technologies for controlled inhalation studies with different atmospheres

Toxicology testing of chemical substances

We offer a broad range of toxicological tests enabling assessment of potential risks from chemicals, particles, complex mixtures, and nanomaterials. Depending on our clients' specific requirements, we develop appropriate testing strategies and, if required, conduct toxicology studies with different routes of administration – with a focus on inhalation toxicology and characterization of inhalable substances. Our service portfolio includes:

- Regulatory assessment by means of standard toxicological tests in compliance with international guidelines (OECD, EU, EPA, or FDA)
- P.R.I.T.[®] exposure system for in-vitro exposure of cells and tissues to airborne, soluble, and particulate test substances at air/liquid interfaces
- Characterization of molecular mechanisms of action
- Use of our own toxicological databases (RITA, goRENI, DevTox)



Exposure characterization

To characterize occupational, indoor, and environmental human exposure to gases and aerosols/particles, inhalation exposure in particular, we combine state-of-the-art measurement technology with mathematical modeling tools. Whenever necessary, we provide adaptations to customize a solution to a client's specific needs or to guarantee its compliance with relevant regulations. We use the following methods for this purpose:

- Physical and chemical measurement of aerosol and vapor emissions such as dusts, (nano)particles, sprays, oil mists and vapors, and microorganisms
- Exposure modeling, calculation, and measurement: quantification and dispersion of pollutants (e.g. by modeling in SprayExpo), measurement methods for spray applications, deposition and absorption modeling, exposure calculation based on existing models
- Development of custom measurement and process technology for dusts and aerosols (PM₁₀, PM_{2,5}, exhaust gases, nanoparticles)
- Aerosol generation methods (calibration aerosols, nebulization, dry dispersion)
- Process development: development of test methods and analytical procedures

Regulatory research and risk assessment of chemicals

To assess the potential risk from chemical substances – industrial chemicals, biocides, food additives, and human and veterinary medicinal products – including their use in specific products, we use a tiered approach, referred to as integrated testing strategy (ITS). With self-initiated research projects, we contribute to the development of novel assessment strategies to help improve and refine existing risk assessment methods and ultimately to minimize the need for experimental studies, in particular animal studies. Examples of such projects are elucidation of structure-activity relationships ((Q)SAR), category approaches such as read across, the setting up of databases, and further development of the TTC concept.

For risk assessment of chemicals and their registration for a particular use, we offer:

- Data gap analysis and literature search: in cooperation with the sponsor, we determine what data are available and whether additional studies are necessary, and we check whether there is information publicly available about the substance in question.
- Preparation of dossiers: we prepare IUCLID-5 datasets for the studies, perform exposure and risk assessments, and prepare a chemical safety report (CSR) and the registration dossier.
- Consulting and support to develop a registration strategy tailored to your situation.
- Experimental investigations, e.g. for toxicology testing, can be performed directly at Fraunhofer ITEM or are subcontracted to other testing institutes. If an external partner is needed, we can assist you in selecting an appropriate partner and in the monitoring of your studies.
- Risk assessment and expert reports: in the form of expert reports, we document the (eco)toxicological properties of substances and assess their risks to human health and the environment, for example for REACH registrations, for biocides, and for contaminations or chemical residues in foods and products.

PROJECTS

Risks from pyrrolizidine alkaloids in foods

Due to their toxic potential, pyrrolizidine alkaloids (PA) are unwanted in food products. About three percent of all blossoming plants contain these compounds which serve mostly as protection against herbivores. There are more than 660 pyrrolizidines, about half of which display hepatotoxic effects. The German Federal Institute for Risk Assessment (BfR) has provisionally assessed the risk arising from food products, tea and honey in particular, and recommended a daily dose ≤ 7 ng for 1,2-unsaturated PA. The following structural features are characteristic for the typical toxic effects of PA on the liver and partly also on the lung: PA with 1,2-unsaturated necine structure esterified with at least one branched C₅-carboxylic acid

are associated with hepatotoxic, carcinogenic, and mutagenic effects upon cleavage by mixed-function oxidases. Pyrroles of this type are highly reactive alkylating agents that can react with nucleophilic groups of nucleic acids and proteins to form adducts. On behalf of BfR, Fraunhofer ITEM is conducting a 28-day oral toxicity study with six different PA. BfR scientists are performing DNA microarray analyses, while Fraunhofer ITEM scientists are carrying out hematological and histopathological examinations of liver and lung. The results of this study will be used for toxicological assessment of PA.



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DevTox website available in Chinese

The long established DevTox website (www.devtox.org), operated by Fraunhofer ITEM, provides the internationally harmonized nomenclature for anomalies observed in developmental toxicology as a reference in hazard and risk evaluation of chemicals, illustrated by numerous images. Recent enhancements include the harmonized categorization for all findings added in the course of the nomenclature update in 2012 and the translation into Chinese characters. The latter is intended to promote the use of recognized nomenclature by experts in China and to support training. An important precondition for this enhancement was an adjustment of the heterogeneous website for multilingual use, allowing all elements including buttons and program components to be combined to a

uniform Web page in the selected language. The texts were translated into Chinese by cooperators from the Shanghai Institute of Planned Parenthood Research, the WHO Collaborating Centre, and Fudan University. After completion of the technical implementation and thorough testing, the Chinese version was made available to the public and representatives of the cooperation partners German Federal Institute for Risk Assessment, Charité Berlin, and Fraunhofer ITEM presented the DevTox project at the Annual Conference of the Shanghai Society of Environmental Mutagens on November 1, 2016.



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E-cigarette in the laboratory.

Test of a method to identify novel chemical risks in the food chain

On behalf of the European Food Safety Authority (EFSA), Fraunhofer ITEM and FoBiG cooperated in testing a method to identify substances that could pose potential risks to the food chain. This method is based on data from registrations under REACH. The project report is available via the ECHA website (please refer to "Publications": Bitsch et al., 2016). A set of 100 data-rich substances was selected for the test according to a variety of criteria including tonnage ($\geq 1\,000$ t/a) and NOAEL distribution in repeated-dose studies. Four additional substances were selected as positive controls. The data available for these substances were extracted and assessed in six thematic blocks covering environmental exposure, biodegradation, accumulation in foods, repeated-dose toxicity, genotoxicity, carcinogenicity, reproductive and developmental

Light scattering sensor for the analysis of nanoaerosols

Light scattering is a widely used method in aerosol measurement, in particular when high time resolution and ease of operation is required. The light scattering properties of polarized light scattered under an angle of 90 degrees can be used to obtain information on mean particle size and mass concentration of aerosols in the submicron size range. A sensor was developed at Fraunhofer ITEM using a 630-nm laser diode as light source, enabling measurement of the mass concentration and mean particle size of aerosols in the size range between 0.2 and 1.5 μm . The device is particularly useful for process

toxicity. In each block, scores were allocated according to a predefined scoring scheme. Scores were weighted differently in different scenarios and were finally added up to a total score. With regard to the defined criteria, the substances that reached the highest scores could pose potential risks to the food chain and are therefore candidates warranting further investigation of their properties. Besides the use of experimental data, a scoring system enabling prediction of such data has been developed in addition, to allow also evaluation of substances for which data are scarce. In an EFSA follow-up project with official kick-off in January 2017, the partners will apply the tested method to all substances registered under REACH.



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control, since it can be easily integrated into a flow system and its readout is independent of the flow rate drawn through. At Fraunhofer ITEM, the sensor is extensively employed for the characterization of highly concentrated condensation aerosols formed in e-cigarettes. The aerosol formed in a puff can be analyzed in detail with high time resolution. In this context, the sensor is a simple and robust tool for product characterization and optimization.



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Toxicology: in-vitro testing in cell and tissue cultures.

Studies on the hazardousness of carbon nanotubes

Due to their special physical and chemical properties, carbon nanotubes (CNTs) in a large diversity of modifications are put to use in a broad range of innovative processes and products. Human exposure to these materials is possible primarily in manufacturing processes and during treatment and processing. Studies suggest that long and fiber-like CNTs could have tumor-inducing effects similar to those of asbestos fibers. This is why the German Federal Ministry of Education and Research (BMBF) is funding the joint research project "CaNTser". Within this project, potential tumor-causing effects of fiber-like CNTs

after inhalation will be examined at Fraunhofer ITEM. In addition, the mechanism of action of CNTs will be studied by means of gene expression analyses and investigations in cell cultures. The researchers are seeking to identify those features of CNTs that cause, potentiate, or weaken their toxic potential. A main objective of this project is to derive a threshold value for CNTs in order to reduce the risk to humans from exposure to CNTs.



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Cabin air quality in aircraft: investigation completed

Air quality inside airplanes has been a subject of debate for over 60 years. The key issues are the questions whether oil fumes from the engines leak into the cabin and/or cockpit via the bleed air system and, if so, whether they pose a health hazard to airline passengers and crew members. To clarify this issue, the European Aviation Safety Agency (EASA) commissioned Fraunhofer ITEM and the Hannover Medical School (MHH) with a study to measure and analyze in-flight cabin and cockpit air quality. Manpower and logistic support for this project were provided by the companies Lufthansa Technik AG, Condor Flugdienst GmbH, and British Airways. The results of this study are now available. During a total of 69 flights, the scientists monitored numerous potential pollutants such as VOCs, aldehydes, organic phosphorous compounds, carbon monoxide, ozone, carbon dioxide, and also particles and aerosols. The results show only low contamination of cabin air,

which is largely comparable to little contaminated indoor air. Organophosphates such as tricresyl phosphate (TCP) were found only in trace amounts ($< 20 \text{ ng/m}^3$) in cabin air. The distribution of pollutants detected in the bleed air-independent Boeing 787 was in a low range, similar to findings in conventional aircraft. In addition, the high air exchange rate ($> 20/\text{h}$) in aircraft assures rapid dilution of airborne pollutants. In the course of the study, the researchers were able to document a reproducible, characteristic dilution pattern for the individual flight phases, independent of the type of aircraft. In view of these findings, the reported health impairments in connection with fume events are difficult to comprehend. One outcome of this study, therefore, was a recommendation to systematically investigate potential health effects by ethically justifiable human exposure studies.



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Prediction of respiratory toxicity: prevalidation of the ex-vivo model PCLS

In acute inhalation toxicity studies, animals inhale substances at defined concentrations. Without additional information, it is difficult to estimate the appropriate starting concentration for in-vivo inhalation studies. In the context of REACH and the principle of the 3 Rs, there is an increasing public demand for alternative methods. Fraunhofer ITEM was involved in the standardization and prevalidation of precision-cut lung slices (PCLS) as a suitable ex-vivo alternative method to reduce animal numbers in inhalation toxicology. To this end, lung tissue was exposed to increasing concentrations of 20 industrial chemicals in serum-free culture medium under normal submerged culture conditions. Evaluated endpoints included toxicity (WST-1 assay, LDH assay, and BCA assay) and inflammation (IL-1 α). For each endpoint, test acceptance criteria were

established. We recently published the final results for all 20 chemicals (Hess et al. 2016 in Toxicology in Vitro). More than 900 concentration-response curves were analyzed. Results obtained for all assay endpoints showed best intra- and inter-laboratory consistency for the data obtained by WST-1 and BCA assays. While WST-1 and LDH indicated toxic effects for the majority of substances, only some of the substances induced an increase in extracellular IL-1 α . Two prediction models were developed and showed promising results. Whether or not the model will be used for prediction of in-vivo inhalation toxicity remains open, but it certainly provides the opportunity to save animal lives in future.



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PLATOX: validated in-vitro toxicity data of graphene nanoplatelets

Graphene nanoplatelets (GNP) represent a new class of carbon-based nanomaterials, with a thickness dimension in the nanometer range and very attractive technical properties. For example, GNP can increase the mechanical stability and conductivity of composite materials. This is why a variety of GNP have already been introduced to the market, although no adequate risk assessment, for workplaces in particular, has so far been possible, due to the still limited availability of toxicity data. In the PLATOX project, funded under the FP7 SIINN ERA-NET program, three institutions from three European countries have accepted the challenge of generating validated in-vitro data for risk assessment. Fraunhofer ITEM as project coordinator was initially responsible for the selection and physicochemical characteriza-

tion of seven commercially available GNP to be tested. For the ongoing in-vitro tests, Fraunhofer ITEM has been using primary, lung-relevant cell models and both established and innovative endpoints to determine the (geno)toxic and inflammatory potential of the GNP and enable a ranking regarding their toxic potency. To guarantee validity of the generated data, all work steps have to be comprehensively adapted to the special properties of GNP. The in-vivo relevance of the in-vitro data will be verified by using selected GNP in a 28-day inhalation study in rats. All data generated will eventually be used to perform final risk assessment to improve occupational safety.



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TRANSLATIONAL BIOMEDICAL ENGINEERING



OUR SERVICES: FROM IDEA TO SAFE MEDICAL DEVICE

Development of medical devices is a complex process taking place in a highly regulated environment. Besides specific technical expertise in this area, compliance with the relevant regulatory requirements is of pivotal importance. In this environment, we conduct research, development projects, and device testing. Our Translational Biomedical Engineering team has several years of experience in the development of medical devices.

Close dovetailing with the institute's other working groups with scientific or medical focuses allows the team to provide comprehensive support to clients in their development projects, to the point of performing the required pre-clinical and early-phase clinical studies. Cooperation with both internal and external development partners from industry and academia enables flexible responses to project-specific requirements. In the area of quality and risk management, we support qualification of external technology processes.

One focus is on active implants: We develop tailored methods for safety and functionality testing of such implants (in compliance with EN ISO 14791 and ISO 10993) and new accelerated aging models for polymer implants in particular. The second focus is on conducting and assisting the development of novel technologies for administration of medicinal aerosols towards smart drug/device combination products.

The services offered by Fraunhofer ITEM assist you on the way from idea to safe medical device.



Device development and processes suitable for SMEs

Our conceptual development work is reflected in the development of medical devices and test benches. Development of devices is performed either as contract research or supporting other research projects. Whenever required, new test benches are developed in parallel and are made available for testing of newly developed devices. This allows our clients to substantially reduce the obstacles encountered during development of innovative products and the risk of technology transfer failure. Furthermore, within our network we provide biomedical engineering systems for demonstration purposes and prototypes for clinical trials.

Development of active implants: Fraunhofer ITEM scientists are currently developing test methods to determine the long-term behavior of active polymer implants that exceed the known standards of temperature acceleration. Such research is geared towards preventing repeat surgery wherever possible and towards minimizing the risk of implant failure.

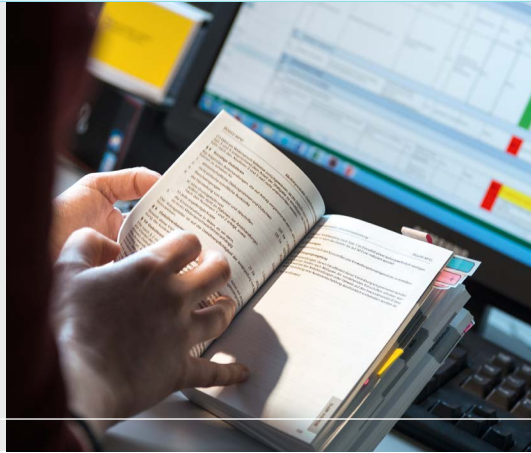
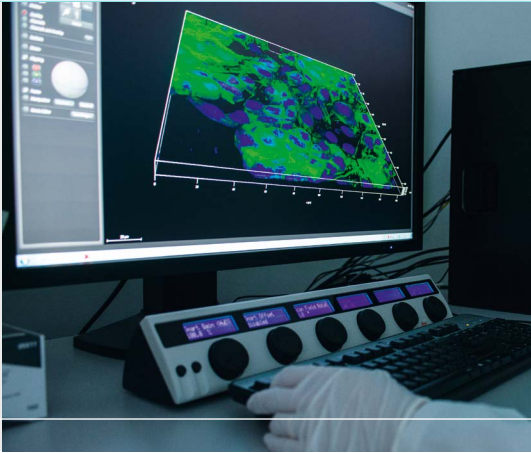
Development of medical inhalers: Medical inhaler technology is increasingly evolving from simple, constant drug administration to intelligent, breathing-controlled systems for inhalation treatment with pharmaceuticals. At Fraunhofer ITEM, we develop products and test benches to the point of meeting the requirements for use in first clinical trials or as validated measurement systems. We are thus able to make an important contribution to your development process: from initial explorative research via prototype manufacturing and verification to the first clinical trials. Our aim is to support above all small and medium-sized enterprises in their development projects.

Testing and testing scenarios

Besides the use of standard methods, a focus here is on the development of novel test methods. These include above all in-vitro accelerated aging models for active implants, which are necessary to allow stability testing of such implants that can be expected to be of long-term durability, within a short time span.

The test systems for medical devices intended for use in aerosol and inhalation therapy follow a risk management approach – the relevant standards such as ISO 20072 do not stipulate the application of particular test methods. For example, when it comes to testing novel inhalers for use in neonates, there is a need to develop new test methods, as there are no suitable test systems available.

Testing of active implants: Modern active implants are basically designed for early childhood implantation and 100-year periods of use. In order to ensure compliance with these requirements already during development, accelerated testing must be employed. Whilst exposure to higher temperatures has been a working solution for many applications, thin-film polymer devices face reliability limits with a pure temperature increase. To solve this problem nonetheless, we develop new test methods that make use of a multi-parameter model with elevated pressure and artificial body fluids at high concentrations. By setting up mathematical modeling in parallel, we are able to additionally substantiate the desired long-term life span forecasts.



Testing of medical inhalers: Testing of novel devices with standard methods is often not possible. This is why relevant standards leave scope for action. ISO 20072, for example, does not stipulate the test method to be used for testing of inhalation devices. Quite the contrary, for novel inhalation systems in many cases it is necessary to follow a risk-based approach and adapt existing or develop new test methods. We use standard methods as well, but our focus is on testing novel devices and especially devices used in inhalation circuits for adults and neonates. This includes not only measurements of device performance, but also investigation of any impact the delivered substance may have on the whole ventilator circuit. This might be, for example, blockage of filters or other air-conducting pathways, such as nasal prongs of neonates.

Safety and risk assessment of medical devices

The clinical use of medical devices requires that this use poses no risk to the safety and health of patients and device users. Consequently, risk management plays a pivotal role in the development of medical devices. Based on our experience, we support our partners throughout the development phase in minimizing any risks in compliance with the relevant standards. We support our partners with our expertise in the development and implementation of safety features, the formal implementation of risk management, and any risk mitigation measures that may be required.

Regulatory support to reach market approval of medical devices

An important pillar for success in the development of medical device technology is the regulatory strategy. The earlier this strategy is established, the shorter the time to market. During startup, the focus is frequently on other important questions; therefore, we offer early support to address relevant regulatory issues, especially to small enterprises and startups. This support includes assistance in the selection of an approval strategy, implementation of this strategy, and workshops to sensitize for processes and documentation necessary for market approval. This is particularly important, given that the currently still valid Medical Device Directive will soon be replaced by the much more stringent EU-wide Medical Device Regulation.

PROJECTS

Breath-activated administration of dry-powder aerosol to ventilated patients

In the local treatment of lung infections (caused by bacteria or fungi) there is a considerable medical need for local delivery of high doses of active pharmaceutical ingredients (APIs). With up to several 100 mg of API per day, the required local pulmonary dose in this case is two to three orders of magnitude higher than in "traditional" inhalation treatment. In this context, there is an urgent need for further development both of portable and stationary inhalers for use by patients themselves and in particular for the development of aerosol dosing methods for use in combination with ventilation systems in intensive care. For children in particular, their lacking coordination capacities

and changes in lung anatomy and breathing mechanics throughout childhood require the development of automated systems that are able to adapt to the individual situation. Sensory in-situ breath monitoring and adjustment of the administered dose thus have to be closely coupled. The development activities at Fraunhofer ITEM are addressing these needs with a system that doses the medical aerosol by means of a miniaturized aerosol valve in the patient's nosepiece or mouthpiece, controlled based on respiratory mechanics monitoring.



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Innovative antimicrobial shield for implants

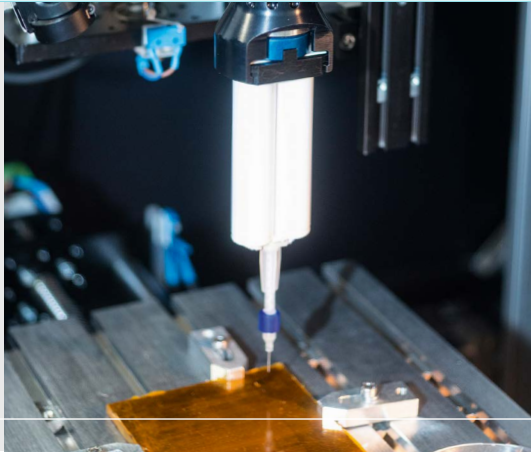
Insertion of implants, for example of hip or knee endoprostheses, poses the risk of infection and resulting dysfunction of the implant. Such problems are caused by bacteria colonizing the implant surface and subsequently forming a biofilm that is resistant to antibiotic treatment. This is why scientists are investigating in depth potential modifications of implant surfaces, aimed at preventing bacterial colonization. The Fraunhofer-Gesellschaft is internally funding the project "SynergyBoost", in which the Fraunhofer Institutes IFAM, IME, IZI and ITEM are collaborating to develop novel implant coatings. Due to a combination of antibiotics and silver, these coatings shall be more effective than the products so far available. At Fraunhofer ITEM, the newly developed implant surfaces will be colonized in vitro with the typical bacterial strain *Staphylo-*

coccus aureus and their antibacterial efficacy will be tested. Further investigations in animal models are also part of the project. In addition to efficacy testing, Fraunhofer ITEM scientists will accompany the development of novel implant coatings to comply with the relevant standards and guidelines, e.g. DIN EN ISO 10993 and DIN EN ISO 14971. To this end, they will create the technical documentation required to apply for marketing approval of this innovative drug/technology combination. The project will further enhance Fraunhofer ITEM's expertise in its newly established Business Unit "Translational Biomedical Engineering", where it offers companies and also academic institutions support and assistance in the development of medical devices.



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The novel 3D printing technique enables production of medical silicon elastomers.

FINAMI project: development of plug connectors for neuro-implants

In the FINAMI (Flexible Individualized Active Medical Implants) project funded by the German Federal Ministry for Economic Affairs and Energy, a consortium of industry and research partners is developing reversible plug connectors for lifetime flexible active medical implants. Within this project, Fraunhofer ITEM is developing a test bench for accelerated life cycle testing, where the aging process of active implants can be artificially accelerated to a high degree to enable analysis of material failure. The project partner Hannover Medical School (cluster of excellence "Hearing4all") is contributing a novel 3D printing technique using silicon elastomers. The core of the 3D printing technique is a high-performance infrared laser reducing the vulcanization time of typical silicon elastomers from about

1.5 hours to a few hundred milliseconds. It vulcanizes the silicon elastomer so quickly that the melting this material typically undergoes when heated is almost completely avoided. The 3D printing of silicon elastomers allows, for example, plug connectors (connected during surgical intervention) to be encapsulated safely yet revisably. This 3D printer, which at present has the highest resolution worldwide, is intended to be further developed at Fraunhofer ITEM in close collaboration with the project partner. The aims of this development are to enable production of individualized neuro-implants tailored to each patient and a future scale-up to larger prostheses.



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Novel test method to help select the most appropriate inhaler

Inhalation of therapeutics is a cornerstone in the treatment of patients with respiratory diseases. Drug delivery to the lungs is often facilitated by dry-powder or metered-dose inhalers. For each device, a patient has to meet certain requirements to enable optimal inhalation of the drug. The aim of this study, performed in cooperation with the company Mundipharma GmbH and the hospital Fachkrankenhaus Kloster Grafenschaft, was to get an overview of the requirements customary inhalers place on a patient's breathing power. A doctor in his or her office normally has no access to data on inhaler resistance nor on the patient's breathing power. An unambiguous parameter to evaluate the required and the patient's actual breathing power would facilitate the selection of a suitable inhaler. Another aim of the study, therefore, was to identify a simple

and fast test method to help select the most appropriate inhaler for a particular patient. To this end, the required flow rate of each device was determined by means of a literature search and flow resistance values were measured. These data were used to calculate an optimal and a still acceptable necessary breathing power (P in watts). For the clinical part of the study, the inspiratory flow rate and pressure drop were measured in 21 adults with asthma or COPD and in healthy volunteers, and the peak inspiratory breathing power (PIPO in watts) was then calculated from these measurements. In fact, a single measurement of the PIPO value enables the selection of a suitable inhaler almost independently of the respiratory resistance.



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PERSONALIZED TUMOR THERAPY



OUR SERVICES: FROM MOLECULAR ANALYSIS TO PERSONALIZED THERAPY

The Division of Personalized Tumor Therapy was set up in December 2010 as a research collaboration between the Fraunhofer-Gesellschaft, the *Land* of Bavaria, and the University of Regensburg. Right from the start, the team of scientists in Regensburg had been organizationally attached to Fraunhofer ITEM in Hannover as a project group, funded by the Bavarian government for the first five years. After its successful evaluation in November 2016, the project group was included in the financing model of the Fraunhofer-Gesellschaft and became a Fraunhofer ITEM division in January 2017. The division is headed by Prof. Christoph Klein, who is also holding the Chair of Experimental Medicine and Therapy Research of the University of Regensburg.

The focus of this division is on the development of diagnostic tests and innovative models to enable detection of disseminated cancer cells early in the disease and prediction of the response to therapy of metastatic progenitor cells. The newly developed methods for single-cell analysis enable detection and comprehensive characterization of disseminated cancer cells, which are extremely rare. These analyses will then allow targeted development of systemic therapies that promise to be more effective than the therapies so far available. The Division of Personalized Tumor Therapy has been certified by TÜV Süd according to DIN ISO 9001:2015 and thus complies with international standards.

The services offered by this division can assist you on the way from molecular analysis to personalized tumor therapy.



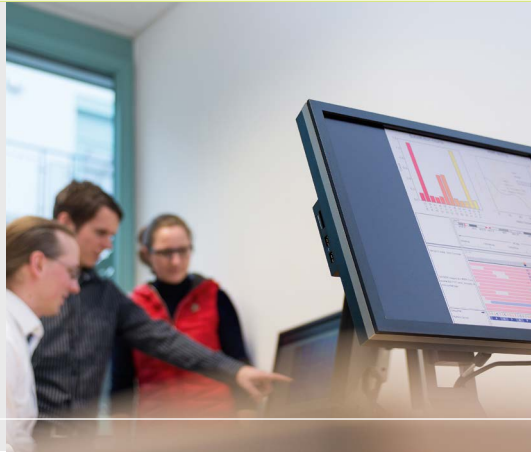
Single-cell analysis

Enrichment, isolation and molecular analysis of rare cells

Our commitment is to drive innovative therapeutic approaches by decoding the underlying mechanisms in complex diseases on a single-cell level. The focus is on solid cancers, e.g. the analysis of circulating tumor cells (CTCs) and disseminated cancer cells (DCCs), however, our technologies can be adjusted to different application areas, such as stem cell therapy. Our expertise ranges from the development and implementation of individual enrichment and staining strategies to the isolation of pure cell populations, down to a single target cell. As an accredited single-cell laboratory and through our cooperation with the University of Regensburg, we have access to a sample biobank generated from single CTCs/DCCs of patients with different cancer types. We use these for biomarker research and target validation, and for many samples a correlation with the clinical follow-up can be established. We thus work in a perfect environment for translational research within clinical studies.

Decoding of single cells

For the development of tailored solutions for single-cell or rare-cell analysis, we offer expert knowledge in next-generation sequencing (NGS) and microarray technologies, in particular at the single-cell DNA and RNA levels. Our in-house developed workflows are optimized for the analysis of clinical low-input or single-cell samples, e.g. cancer cells isolated from body fluids, fine-needle aspirates and tissue specimens. Our workflow integrates quality control assays for optimal sample selection, technical implementation, and bioinformatics evaluation.



Innovative tumor models

In-vitro and in-vivo drug testing

For efficacy testing of drugs in innovative preclinical models representing systemic cancer disease, we offer experience in the generation of cellular models for functional analysis of rare cancer cell populations from fluids, organs, and primary tumors. To this end, we have established technologies allowing expansion of few DCCs or CTCs despite their extremely low abundance. Such preclinical models allow us to perform individualized pharmaceutical drug tests, both in vitro and in vivo, and provide the opportunity to comparatively test drugs on cancer subpopulations.

Advanced preclinical PDX models

Preclinical animal models only partially represent the patient situation. Fraunhofer ITEM in Regensburg is developing optimized PDX (patient-derived xenograft) models allowing more representative preclinical drug testing. Our advanced models are based on patient-derived metastatic precursor cells (DTCs) or circulating tumor cells (CTCs). In addition, we concomitantly generate a human immune system in these models, which infiltrates the human tumors and develops phenotypes (e.g. tumor-associated macrophages) that have been described in patient samples. This allows both the tumor development and the dissemination of cancer cells into different organs to be followed in the presence of human immune cells. Our services include development of individualized preclinical in-vivo models to test in particular immunomodulatory drugs on target cells of systemic disease.

Mathematical modeling and bioinformatics

Multi-level disease modeling

Data analysis and biological process modeling are necessary to facilitate development of innovative therapies and support their clinical application. Therefore, we offer our clients profound data analysis and result visualization as well as aim-oriented mathematical modeling of biological mechanisms, disease progression, and therapeutic effects. We can also assist in experimental planning and statistical evaluation of experiments and patient trials. Our spectrum of methods ranges from feature selection, pattern recognition, machine learning, and network analysis to population dynamics, probability theory, and predictive modeling.

Bioinformatics services

Complex biological questions normally cannot be addressed by generalized "one-fits-all" approaches. Our commitment is to provide tailored bioinformatics solutions that provide a comprehensive yet specific answer to your experimental questions. We offer our clients expertise in bioinformatic analysis of high-throughput data from next-generation sequencing or microarray experiments. The Fraunhofer ITEM bioinformatics experts in Regensburg are focused on analyzing human single-cell omics data. Our expertise ranges from simple gene expression via complex genome reconstruction analyses to the development of novel algorithms and applications. Clients are invited to use our counseling services.

PROJECTS

Development of preclinical models from circulating tumor cells

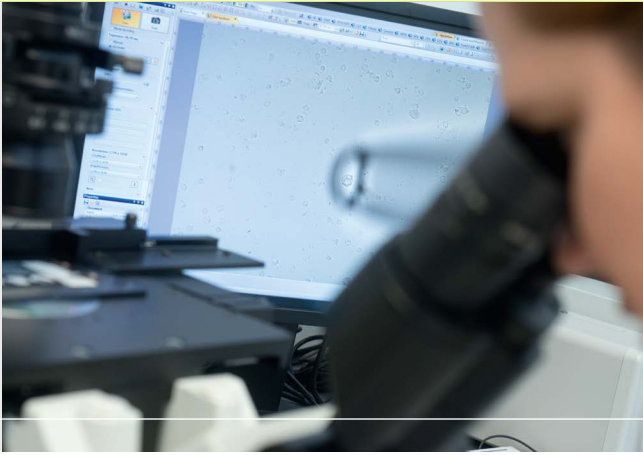
Detection and analysis of circulating tumor cells (CTCs) in peripheral blood from patients with metastatic disease has become a growing focus of biomedical and clinical interest over the past few years – because such disseminated cells can provide important information regarding patient prognosis, disease progression, and the individual's response to therapy. Besides their quantification, molecular characterization allows the genetic profile of these tumor cells to be analyzed, thereby enabling targeted, personalized treatments. Collection of a blood sample for subsequent isolation of tumor cells, a method also referred to as "liquid biopsy", offers an alternative non-invasive diagnostic approach in particular for inoperable solid tumors such as small-cell lung cancer (SCLC), a highly malignant form of bronchial carcinoma. Given that tumor cells of this cancer type in most cases have already spread extensively at the time of diagnosis and furthermore tend to become drug resistant after chemotherapy, SCLC patients so far have a poor chance of survival. Despite modern treatment options, the five-year survival rate with this type of tumor is only about 2 percent. Appropriate cell models mimicking the setting in patients as closely as possible and representing the tumor's molecular properties are thus required to enable development of more efficient therapeutic approaches in the future.

To this end, Fraunhofer ITEM scientists in Regensburg have developed preclinical in-vitro and in-vivo models from patient-derived CTCs, enabling expansion of these important cells. Due to their limited availability (in most cases only 1 to 300 CTCs/ml blood) and cell viability, maintaining the detected CTCs ex vivo in a viable, proliferative state for a prolonged period of time after their isolation poses a great challenge. With the establishment of combined in-vitro and in-vivo approaches, the scientists, therefore, pursued different cultivation strategies. For example, they successfully isolated CTCs from blood samples of two SCLC patients, precultured the cells under optimized conditions, and/or expanded them in a mouse model. Molecular biological analyses showed that these models express SCLC-specific tumor markers such as EpCAM, CD56 or cytokeratin and display the same mutations that can also be found in the patients' genomes, even after prolonged in-vitro or in-vivo cultivation. Furthermore, comparative genomic hybridization, which is a genetic analysis of the whole genome, confirmed that the developed models indeed reflect the molecular properties of patient-derived CTCs. These new cell models thus represent the actual target cells of systemic therapies, enabling research on metastasis formation and mechanisms of drug resistance as well as testing of novel therapeutic approaches to treat SCLC patients.



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Isolation of a single cell using a micromanipulator. The genetic profile of disseminated cancer cells often differs from that of the primary tumor.

New mechanisms of early metastatic spread in breast cancer discovered

Over several decades, cancer research pursued the dogma that cancer cells preferentially seed from advanced tumors. This concept was based on the finding that early surgical removal is decisive for curing cancer patients. Recently, however, the validity of this concept has increasingly been questioned because also patients with small tumors develop metastases. Furthermore, the genetic profile of disseminated cancer cells often does not show the expected similarity to the primary tumor. Disseminated cancer cells, as precursors of metastases, frequently seem to derive from early tumor evolution stages. Another finding that did not match the concept of late dissemination was the observation that the number of disseminated cancer cells did not correlate with primary tumor size. This spawned the hypothesis that large tumors might be less able to metastasize than small tumors.

Scientists of the Regensburg-based Fraunhofer ITEM Division of Personalized Tumor Therapy, the Chair of Experimental Medicine and Therapy Research of the University of Regensburg, both headed by Prof. Christoph Klein, and the Department of Hematology and Oncology, led by Prof. Julio Aguirre-Ghiso, at the Icahn School of Medicine at the Mount Sinai Hospital in New York for the first time ever studied mechanisms of early metastatic spread in breast cancer and recently published their seminal results in the renowned scientific journal "Nature" (Hosseini et al., 2016 and Harper et al., 2016). The researcher teams found that breast cancer formation hijacks physiological processes controlling mammary epithelial branching and mammary stem-cell expansion in adolescence and pregnancy, deregulates and then misuses them for tumor cell dissemination. In early stages of cancer development, characterized by low cell density and moderate activation of the

oncogene HER2, the steroid hormone progesterone led to increased migration of cancer cells and acquisition of so-called stemness properties, both major prerequisites for metastasis. Interestingly, the same hormone suppresses migration and stemness in advanced tumors, with this reversal of effects being mediated by strong activation of HER2, increased cell density, and so-called microRNAs.

The Regensburg researchers were able to demonstrate that at least 80 percent of metastases were derived from early lesions and that their findings, which they mainly obtained from animal models, are also relevant for human metastatic dissemination. The researchers in New York found out that the interactive process between HER2 and the tumor suppressor gene p38 regulates what is referred to as "epithelial-mesenchymal transition", which allows stationary mammary gland cells to acquire migratory capacity, a process that also normally takes place in mammary gland development. The conclusion drawn by the researchers is that metastases probably derive from different stages of primary tumor evolution and that the resulting cell heterogeneity needs to be addressed for future therapies to be successful.



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CONTACTS

Fraunhofer ITEM has pooled the competencies from its various divisions in three business units: Drug Development, Chemical Safety and Assessment, and Translational Biomedical Engineering. Another focus is on personalized tumor therapy, a subject area explored by the scientists of the corresponding Regensburg-based division of Fraunhofer ITEM. Below please find the contacts for the different thematic areas and services offered. Please do not hesitate to contact these persons directly, should you have any questions or needs.

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Dr. Pohlmann and Prof. Doll are also your contacts for the
following subject areas:

Device development and processes suitable for SMEs

Testing and testing scenarios

Safety and risk assessment of medical devices

**Regulatory support for market approval of medical
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Personalized Tumor Therapy

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FRAUNHOFER-GESELLSCHAFT

Research of practical utility lies at the heart of all activities pursued by the Fraunhofer-Gesellschaft. Founded in 1949, the research organization undertakes applied research that drives economic development and serves the wider benefit of society. Its services are solicited by customers and contractual partners in industry, the service sector and public administration.

At present, the Fraunhofer-Gesellschaft maintains 69 institutes and research units. The majority of the 24,500 staff are qualified scientists and engineers, who work with an annual research budget of 2.1 billion euros. Of this sum, 1.9 billion euros is generated through contract research. More than 70 percent of the Fraunhofer-Gesellschaft's contract research revenue is derived from contracts with industry and from publicly financed research projects. Almost 30 percent is contributed by the German federal and state governments in the form of base funding, enabling the institutes to work ahead on solutions to problems that will not become acutely relevant to industry and society until five or ten years from now.

International collaborations with excellent research partners and innovative companies around the world ensure direct access to regions of the greatest importance to present and future scientific progress and economic development.

With its clearly defined mission of application-oriented research and its focus on key technologies of relevance to the future, the Fraunhofer-Gesellschaft plays a prominent role in the German and European innovation process. Applied research has a knock-on effect that extends beyond the direct benefits perceived by the customer: Through their research and development work, the Fraunhofer Institutes help to reinforce the competitive strength of the economy in their local region, and throughout Germany and Europe. They do so by promoting innovation, strengthening the technological base, improving the acceptance of new technologies, and helping to train the urgently needed future generation of scientists and engineers.

As an employer, the Fraunhofer-Gesellschaft offers its staff the opportunity to develop the professional and personal skills that will allow them to take up positions of responsibility within their institute, at universities, in industry and in society. Students who choose to work on projects at the Fraunhofer Institutes have excellent prospects of starting and developing a career in industry by virtue of the practical training and experience they have acquired.

The Fraunhofer-Gesellschaft is a recognized non-profit organization that takes its name from Joseph von Fraunhofer (1787–1826), the illustrious Munich researcher, inventor and entrepreneur.

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FRAUNHOFER-INTERNAL NETWORKING

Fraunhofer Institutes working in related subject areas cooperate in Fraunhofer Groups dedicated to specific topics and fostering a joint presence on the R&D market. The Fraunhofer Alliances facilitate customer access to the services and research results of the Fraunhofer-Gesellschaft. Common points of contact for groups of institutes or departments active in related fields provide expert advice on complex issues and coordinate the development of appropriate solutions along the entire value chain. Fraunhofer Institutes furthermore cooperate in Fraunhofer research projects. For example, Fraunhofer ITEM is a member of the Fraunhofer Group for Life Sciences and the Fraunhofer Nanotechnology Alliance and collaborates with other Fraunhofer Institutes in the joint research project RIBOLUTION. Fraunhofer ITEM is thus well networked in the Fraunhofer-Gesellschaft – successful research requires scientific exchange.

Fraunhofer Group for Life Sciences

Six Fraunhofer Institutes and a Fraunhofer Research Institution, each having proven in-depth expertise in different areas within the life sciences, are involved in this Group: the Fraunhofer Institutes for Biomedical Engineering IBMT, Interfacial Engineering and Biotechnology IGB, Molecular Biology and Applied Ecology IME, Toxicology and Experimental Medicine ITEM, Process Engineering and Packaging IVV, Cell Therapy and Immunology IZI, and the Fraunhofer Research Institution for Marine Biotechnology and Cell Technology EMB. Their combined knowledge of biology, chemistry, biochemistry, biotechnology, medicine, pharmacology, ecology, and nutritional science is pooled and synergized within this Fraunhofer Group. In all these Fraunhofer institutions, the scientists collaborate in interdisciplinary teams, so that tailored know-how concerning information technology, engineering science, and legal requirements is also available. Research and implementation at the client's facilities thus go hand in hand.

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Fraunhofer Nanotechnology Alliance

The Fraunhofer Nanotechnology Alliance covers the whole R&D value chain from application-oriented research to industrial implementation. A focus is on multifunctional coatings for use in the optical, automotive and electronics industries. Special nanoparticles (metals, oxides etc.), carbon nanotubes and nanocomposites are designed and used for actuators, structural materials, and biomedical applications. The Alliance furthermore deals with issues of toxicology and safe handling of nanoparticles – this is where Fraunhofer ITEM is bringing in its expertise. The institutes of this Alliance have focused their activities on the following main topics: nanomaterials, nanobiotechnology, nanoprocessing and handling, nanooptics and electronics, measuring methods and techniques, and technology transfer and consulting.

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Research project RIBOLUTION

In the Fraunhofer research project RIBOLUTION, five Fraunhofer Institutes are taking an innovative approach to biomarker screening for modern diagnostic solutions. Their aim is to identify novel biomarkers based on ribonucleic acids that can serve as diagnostic indicators or enable prediction of disease progression or future response to therapy, and develop these to the point of clinical proof of concept with the aid of selected patient cohorts. Fraunhofer ITEM is screening for biomarkers that may serve as diagnostic indicators of chronic obstructive pulmonary disease (COPD), enable monitoring of this disease or prediction of its response to therapy.

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Publications

- Alberter, B.; Klein, C. A.; Polzer, B.
Single-cell analysis of CTCs with diagnostic precision: opportunities and challenges for personalized medicine.
In: *Expert Review of Molecular Diagnostics* 16 (2016), No. 1, pp. 25-38.
doi: 10.1586/14737159.2016.1121099
- Allers, M.; Langejuergen, J.; Gaida, A.; Holz, O.; Schuchardt, S.; Hohlfeld, J. M.; Zimmermann, S.
Measurement of exhaled volatile organic compounds from patients with chronic obstructive pulmonary disease (COPD) using closed gas loop GC-IMS and GC-APCI-MS.
In: *Journal of Breath Research* 10 (2016), No. 2, p. 026004.
doi: 10.1088/1752-7155/10/2/026004
- Api, A. M.; Belsito, D.; Bhatia, S.; Botelho, D.; Browne, D.; Bruze, M.; Burton, G. A., Jr.; Buschmann, J.; Calow, P.; Dagli, M. L.; Date, M.; Dekant, W.; Deodhar, C.; Fryer, A. D.; Joshi, K.; Kromidas, L.; La Cava, S.; Lalko, J. F.; Lapczynski, A.; Liebler, D. C.; O'Brien, D.; Parakhia, R.; Patel, A.; Penning, T. M.; Politano, V. T.; Ritacco, G.; Romine, J.; Salvito, D.; Schultz, T. W.; Shen, J.; Sipes, I. G.; Thakkar, Y.; Tsang, S.; Wahler, J.; Wall, B.; Wilcox, D. K.
RIFM fragrance ingredient safety assessment, elemol, CAS Registry Number 639-99-6.
In: *Food and Chemical Toxicology* (2016) [epub ahead of print].
doi: 10.1016/j.fct.2016.11.027
- Api, A. M.; Belsito, D.; Bhatia, S.; Bruze, M.; Burton, G. A., Jr.; Buschmann, J.; Calow, P.; Dagli, M. L.; Dekant, W.; Fryer, A. D.; Kromidas, L.; La Cava, S.; Lapczynski, A.; Liebler, D. C.; O'Brien, D.; Parakhia, R.; Penning, T. M.; Politano, V. T.; Ritacco, G.; Salvito, D.; Schultz, T. W.; Shen, J.; Sipes, I. G.; Wall, B.; Wilcox, D. K.
RIFM fragrance ingredient safety assessment, 2-Hydroxy- $\alpha,\alpha,4$ -trimethylcyclohexanemethanol, CAS Registry Number 42822-86-6.
In: *Food and Chemical Toxicology* 97S (2016), pp. S209-S215.
doi: 10.1016/j.fct.2016.10.009
- Api, A. M.; Belsito, D.; Botelho, D.; Bruze, M.; Burton, G. A.; Buschmann, J.; Calow, P.; Dagli, M. L.; Dekant, W.; Fryer, A. D.; La Cava, S.; Lapczynski, A.; Liebler, D. C.; O'Brien, D.; Parakhia, R.; Patel, A.; Penning, T. M.; Ritacco, G.; Romine, J.; Salvito, D.; Schultz, T. W.; Sipes, I. G.; Wahler, J.
RIFM fragrance ingredient safety assessment, β -Guaiene, CAS Registry Number 88-84-6.
In: *Food and Chemical Toxicology* (2016) [epub ahead of print].
doi: 10.1016/j.fct.2016.11.017
- Batke, M.; Gütlein, M.; Partosch, F.; Gundert-Remy, U.; Helma, C.; Kramer, S.; Maunz, A.; Seeland, M.; Bitsch, A.
Innovative strategies to develop chemical categories using a combination of structural and toxicological properties.
In: *Frontiers in Pharmacology* 7 (2016), Art. 321, 19 pp.
doi: 10.3389/fphar.2016.00321
- Behrsing, H.; Raabe, H.; Manuppello, J.; Bombick, B.; Curren, R.; Sullivan, K.; Sethi, S.; Phipps, R.; Tesfaigzi, Y.; Yan, S.; D'Ruiz, C.; Tarran, R.; Constant, S.; Phillips, G.; Gaca, M.; Hayden, P.; Cao, X.; Mathis, C.; Hoeng, J.; Braun, A.; Hill, E.
Assessment of in-vitro COPD models for tobacco regulatory science: Workshop proceedings, conclusions and paths forward for in-vitro model use.
In: *ATLA Alternatives to Laboratory Animals* 44 (2016), No. 2, pp. 129-66.
- Bitsch, A.; Bohlen, M.-L.; Escher, S.; Licht, O.; Oltmanns, J.; Schneider, K.; Wibbertmann, A.
Final report: Testing a procedure for the identification of emerging chemical risks in the food chain.
External scientific report. OC/EFSA/SCER/2014/03
doi: 10.2903/sp.efsa.2016.EN-1050
- Bleyer, M.; Curths, C.; Dahlmann, F.; Wichmann, J.; Bauer, N.; Moritz, A.; Braun, A.; Knauf, S.; Kaup, F. J.; Gruber-Dujardin, E.
Morphology and staining behavior of neutrophilic and eosinophilic granulocytes of the common marmoset (*Callithrix jacchus*).
In: *Experimental and Toxicologic Pathology* 68 (2016), No. 6, pp. 335-343.
doi: 10.1016/j.etp.2016.05.002
- Bonella, F.; Kreuter, M.; Hagemeyer, L.; Neurohr, C.; Keller, C.; Kohlhaeufel, M. J.; Müller-Quernheim, J.; Milger, K.; Prasse, A.; on behalf of the German Nintedanib Compassionate Use Consortium.
Insights from the German compassionate use program of nintedanib for the treatment of idiopathic pulmonary fibrosis.
In: *Respiration* 92 (2016), No. 2, pp. 98-106.
doi: 10.1159/000448288
- Booth, J. L.; Duggan, E. S.; Patel, V. I.; Langer, M.; Wu, W.; Braun, A.; Coggeshall, K. M.; Metcalf, J. P.
Bacillus anthracis spore movement does not require a carrier cell and is not affected by lethal toxin in human lung models.
In: *Microbes and Infection* 18 (2016), No. 10, pp. 615-626.
doi: 10.1016/j.micinf.2016.06.004

- Bundschuh, M.; Hahn, T.; Ehrlich, B.; Holtge, S.; Kreuzig, R.; Schulz, R. Acute toxicity and environmental risks of five veterinary pharmaceuticals for aquatic macroinvertebrates. In: *Bulletin of Environmental Contamination and Toxicology* 96 (2016), No. 2, pp. 139-43. doi: 10.1007/s00128-015-1656-8
- Calverley, P. M.; Könen-Bergmann, M.; Richard, F.; Bell, S.; Hohlfeld, J. M. Tiotropium Respimat® versus HandiHaler®: comparison of bronchodilator efficacy of various doses in clinical trials. In: *Advances in Therapy* 33 (2016), No. 5, pp. 786-93. doi: 10.1007/s12325-016-0322-9
- Creutzenberg, O.; Kock, H.; Schaudien, D. Translocation and biokinetic behavior of nanoscaled europium oxide particles within 5 days following an acute inhalation in rats. In: *Journal of Applied Toxicology* 36 (2016), No. 3, pp. 474-8. doi: 10.1002/jat.3259
- Deus, D.; Kehrenberg, C.; Schaudien, D.; Klein, G.; Krischek, C. Effect of a nano-silver coating on the quality of fresh turkey meat during storage after modified atmosphere or vacuum packaging. In: *Poultry Science* (2016) [pub ahead of print]. doi: 10.3382/ps/pew308
- Dunkhorst, W.; Lipowicz, P.; Koch, W. Characterization of highly concentrated organic aerosols by optical extinction in the mid infrared regime: application to e-cigarettes. In: *Journal of Aerosol Science* 94 (2016), pp. 33-42. doi: 10.1016/j.jaerosci.2015.12.004
- Ebinger, S.; Ozdemir, E. Z.; Ziegenhain, C.; Tiedt, S.; Castro Alves, C.; Grunert, M.; Dworzak, M.; Lutz, C.; Turati, V. A.; Enver, T.; Horny, H. P.; Sotlar, K.; Parekh, S.; Spiekermann, K.; Hiddemann, W.; Schepers, A.; Polzer, B.; Kirsch, S.; Hoffmann, M.; Knapp, B.; Hasenauer, J.; Pfeifer, H.; Panzer-Grumayer, R.; Enard, W.; Gires, O.; Jeremias, I. Characterization of rare, dormant, and therapy-resistant cells in acute lymphoblastic leukemia. In: *Cancer Cell* (2016) [pub ahead of print]. doi: 10.1016/j.ccell.2016.11.002
- Elmore, S. A.; Dixon, D.; Hailey, J. R.; Harada, T.; Herbert, R. A.; Maronpot, R. R.; Nolte, T.; Rehg, J. E.; Rittinghausen, S.; Rosol, T. J.; Satoh, H.; Vidal, J. D.; Willard-Mack, C. L.; Creasy, D. M. Recommendations from the INHAND apoptosis/necrosis working group. In: *Toxicologic Pathology* 44 (2016), No. 2, pp. 173-88. doi: 10.1177/0192623315625859
- Fernando, R. N.; Chaudhari, U.; Escher, S. E.; Hengstler, J. G.; Hescheler, J.; Jennings, P.; Keun, H. C.; Kleinjans, J. C.; Kolde, R.; Kollipara, L.; Kopp-Schneider, A.; Limonciel, A.; Nemade, H.; Nguemo, F.; Peterson, H.; Prieto, P.; Rodrigues, R. M.; Sachinidis, A.; Schafer, C.; Sickmann, A.; Spitkovsky, D.; Stober, R.; van Breda, S. G.; van de Water, B.; Vivier, M.; Zahedi, R. P.; Vinken, M.; Rogiers, V. "Watching the Detectives" report of the general assembly of the EU project DETECTIVE Brussels, 24-25 November 2015. In: *Archives of Toxicology* 90 (2016), No. 6, pp. 1529-39. doi: 10.1007/s00204-016-1719-6
- Fossey, S.; Vahle, J.; Long, P.; Schelling, S.; Ernst, H.; Boyce, R. W.; Jollette, J.; Bolon, B.; Bendele, A.; Rinke, M.; Healy, L.; High, W.; Roth, D. R.; Boyle, M.; Leininger, J. Nonproliferative and proliferative lesions of the rat and mouse skeletal tissues (bones, joints, and teeth). In: *Journal of Toxicologic Pathology* 29 (2016), No. 3, Suppl., pp. 49S-103S. doi: 10.1293/tox.29.3S-2
- Gaida, A.; Holz, O.; Nell, C.; Schuchardt, S.; Lavae-Mokhtari, B.; Kruse, L.; Boas, U.; Langejuergen, J.; Allers, M.; Zimmermann, S.; Vogelmeier, C.; Koczulla, A. R.; Hohlfeld, J. M. A dual-center study to compare breath volatile organic compounds from smokers and non-smokers with and without COPD. In: *Journal of Breath Research* 10 (2016), No. 2, p. 026006. doi: 10.1088/1752-7155/10/2/026006
- Gilfanov, A. K.; Koch, W.; Zaripov, S. K. Mathematical modeling of di-ethyl-hexyl-sebacate nanoparticle formation in a free turbulent jet under high nucleation rate conditions. In: *Journal of Aerosol Science* 96 (2016), pp. 124-139. doi: 10.1016/j.jaerosci.2016.02.004
- Gong, Y.; Capstick, M.; Dasenbrock, C.; Fedrowitz, M.; Cobaleda, C.; Sanchez-Garcia, I.; Kuster, N. Comparative dosimetry for children and rodents exposed to extremely low-frequency magnetic fields. In: *Bioelectromagnetics* 37 (2016), No. 5, pp. 310-22. doi: 10.1002/bem.21976
- Gong, Y.; Capstick, M.; Tillmann, T.; Dasenbrock, C.; Samaras, T.; Kuster, N. Desktop exposure system and dosimetry for small-scale in-vivo radiofrequency exposure experiments. In: *Bioelectromagnetics* 37 (2016), No. 1, pp. 49-61. doi: 10.1002/bem.21950
- Gundlach, E.; Hoffmann, M. M.; Prasse, A.; Heinzelmann, S.; Ness, T. Interleukin-2 receptor and angiotensin-converting enzyme as markers for ocular sarcoidosis. In: *PLOS ONE* 11 (2016), No. 1, p. e0147258. doi: 10.1371/journal.pone.0147258
- Gužvić, M.; Klein, C. A. Towards prevention of metastatic prostate cancer: recent molecular insights from the direct analysis of metastatic precursor cells. In: *Translational Cancer Research* 5 (2016), No. S2, pp. S182-S186. doi: 10.21037/tcr.2016.07.28
- Hackner, K.; Erhalt, P.; Mueller, M. R.; Speiser, M.; Marzluf, B. A.; Schulheim, A.; Schenk, P.; Bilek, J.; Doll, T. Canine scent detection for the diagnosis of lung cancer in a screening-like situation. In: *Journal of Breath Research* 10 (2016), No. 4, p. 046003. doi: 10.1088/1752-7155/10/4/046003
- Harper, K. L.; Sosa, M. S.; Entenberg, D.; Hosseini, H.; Cheung, J. F.; Nobre, R.; Avivar-Valderas, A.; Nagi, C.; Girnius, N.; Davis, R. J.; Farias, E. F.; Condeelis, J.; Klein, C. A.; Aguirre-Ghiso, J. A. Mechanism of early dissemination and metastasis in Her2+ mammary cancer. In: *Nature* 540 (2016), No. 7634, pp. 588-592. doi: 10.1038/nature20609
- Heinrichs, M.; Ernst, H. Spontaneous malignant craniopharyngioma in an aged Wistar rat. In: *Journal of Toxicologic Pathology* 29 (2016), No. 3, pp. 195-199. doi: 10.1293/tox.2016-0004
- Hess, A.; Wang-Lauenstein, L.; Braun, A.; Kolle, S. N.; Landsiedel, R.; Liebsch, M.; Ma-Hock, L.; Pirow, R.; Schneider, X.; Steinfath, M.; Vogel, S.; Martin, C.; Sewald, K. Prevalidation of the ex-vivo model PCLS for prediction of respiratory toxicity. In: *Toxicology In Vitro* 32 (2016), pp. 347-361. doi: 10.1016/j.tiv.2016.01.006
- Honti, M.; Hahn, S.; Hennecke, D.; Junker, T.; Shrestha, P.; Fenner, K. Bridging across OECD 308 and 309 data in search of a robust biotransformation indicator. In: *Environmental Science & Technology* 50 (2016), No. 13, pp. 6865-72. doi: 10.1021/acs.est.6b01097
- Hosseini, H.; Obradovic, M. M.; Hoffmann, M.; Harper, K. L.; Sosa, M. S.; Werner-Klein, M.; Nanduri, L. K.; Werno, C.; Ehrl, C.; Maneck, M.; Patwary, N.; Haunschild, G.; Guzvic, M.; Reimelt, C.; Grauvogl, M.; Eichner, N.; Weber, F.; Hartkopf, A. D.; Taran, F. A.; Brucker, S. Y.; Fehm, T.; Rack, B.; Buchholz, S.; Spang, R.; Meister, G.; Aguirre-Ghiso, J. A.; Klein, C. A. Early dissemination seeds metastasis in breast cancer. In: *Nature* 540 (2016), No. 7634, pp. 552-558 [pub ahead of print]. doi: 10.1038/nature20785
- Kerrin, A.; Fitch, P.; Errington, C.; Kerr, D.; Waxman, L.; Riding, K.; McCormack, J.; Mehendele, F.; McSorley, H.; MacKenzie, K.; Wronski, S.; Braun, A.; Levin, R.; Theilen, U.; Schwarze, J. Differential lower airway dendritic cell patterns may reveal distinct endotypes of RSV bronchiolitis. In: *Thorax* (2016) [pub ahead of print]. doi: 10.1136/thoraxjnl-2015-207358
- Kuo, C. S.; Pavlidis, S.; Loza, M.; Baribaud, F.; Rowe, A.; Pandis, I.; Hoda, U.; Rossios, C.; Sousa, A.; Wilson, S. J.; Howarth, P.; Dahlen, B.; Dahlen, S. E.; Chanez, P.; Shaw, D.; Krug, N.; Sandstrom, T.; De Meulder, B.; Lefaudeaux, D.; Fowler, S.; Fleming, L.; Corfield, J.; Auffray, C.; Sterk, P. J.; Djukanovic, R.; Guo, Y.; Adcock, I. M.; Chung, K. F.; on behalf of the U-BIOPRED Project Team. A transcriptome-driven analysis of epithelial brushings and bronchial biopsies to define asthma phenotypes in U-BIOPRED. In: *American Journal of Respiratory and Critical Care Medicine* (2016) [pub ahead of print]. doi: 10.1164/rccm.201512-2452OC
- Lamb, D. J.; Wollin, S. L.; Schnapp, A.; Bischoff, D.; Erb, K. J.; Bouyssou, T.; Guilliard, B.; Strasser, C.; Wex, E.; Blum, S.; Thaler, E.; Nickel, H.; Radmacher, O.; Haas, H.; Swantek, J. L.; Souza, D.; Canfield, M.; White, D.; Panzenbeck, M.; Kashem, M. A.; Sanville-Ross, M.; Kono, T.; Sewald, K.; Braun, A.; Obernolte, H.; Danov, O.; Schaenzle, G.; Rast, G.; Maier, G. M.; Hoffmann, M. BI 1002494, a novel potent and selective oral SYK inhibitor displays differential potency in human basophils and B-cells. In: *Journal of Pharmacology and Experimental Therapeutics* 357 (2016), No. 3, pp. 554-561. doi: 10.1124/jpet.116.233155

- Le, D. D.; Funck, U.; Wronski, S.; Heck, S.; Tschernig, T.; Bischoff, M.; Sester, M.; Herr, C.; Bals, R.; Welte, T.; Braun, A.; Dinh, Q. T. Steroid treatment reduces allergic airway inflammation and does not alter the increased numbers of dendritic cells and calcitonin gene-related peptide-expressing neurons in airway sensory ganglia. In: *Neuroimmunomodulation* 23 (2016), No. 1, pp. 18-26. doi: 10.1159/000440622
- Lefauieux, D.; De Meulder, B.; Loza, M. J.; Peffer, N.; Rowe, A.; Baribaud, F.; Bansal, A. T.; Lutter, R.; Sousa, A. R.; Corfield, J.; Pandis, I.; Bakke, P. S.; Caruso, M.; Chanez, P.; Dahlen, S. E.; Fleming, L. J.; Fowler, S. J.; Horvath, I.; Krug, N.; Montuschi, P.; Sanak, M.; Sandstrom, T.; Shaw, D. E.; Singer, F.; Sterk, P. J.; Roberts, G.; Adcock, I. M.; Djukanovic, R.; Auffray, C.; Chung, K. F.; and the U-BIOPRED Study Group. U-BIOPRED clinical adult asthma clusters linked to a subset of sputum omics. In: *Journal of Allergy and Clinical Immunology* (2016) [epub ahead of print]. doi: 10.1016/j.jaci.2016.08.048
- Lueer, K.; Biller, H.; Casper, A.; Windt, H.; Mueller, M.; Badorrek, P.; Haefner, D.; Framke, T.; Koch, A.; Ziehr, H.; Krug, N.; Koch, W.; Hohlfeld, J. M. Safety, efficacy and repeatability of a novel house dust mite allergen challenge technique in the Fraunhofer allergen challenge chamber. In: *Allergy* 71 (2016), No. 12, pp. 1693-1700. doi: 10.1111/all.12947
- Mangelsdorf, I.; Kleppe, S. N.; Heinzow, B.; Sagunski, H. Indoor air guide values for glycol ethers and glycol esters – a category approach. In: *International Journal of Hygiene and Environmental Health* 219 (2016), No. 4-5, pp. 419-36. doi: 10.1016/j.ijheh.2016.04.006
- May, M.; Drost, W.; Germer, S.; Juffernholz, T.; Hahn, S. Evaluation of acute-to-chronic ratios of fish and *Daphnia* to predict acceptable no-effect levels. In: *Environmental Sciences Europe* 28 (2016), No. 1, pp. 16. doi: 10.1186/s12302-016-0084-7
- May, M.; Drost, W.; Germer, S.; Juffernholz, T.; Hahn, S. Evaluation of the integrated testing strategy for PNEC derivation under REACH. In: *Regulatory Toxicology and Pharmacology* 78 (2016), pp. 59-65. doi: 10.1016/j.yrtph.2016.04.004
- Meinlschmidt, P.; Schweiggert-Weisz, U.; Brode, V.; Eisner, P. Enzyme-assisted degradation of potential soy protein allergens with special emphasis on the technofunctionality and the avoidance of a bitter taste formation. In: *LWT – Food Science and Technology* 68 (2016), pp. 707-716. doi: 10.1016/j.lwt.2016.01.023
- Nendza, M.; Wenzel, A.; Muller, M.; Lewin, G.; Simetska, N.; Stock, F.; Arning, J. Screening for potential endocrine disruptors in fish: evidence from structural alerts and in-vitro and in-vivo toxicological assays. In: *Environmental Sciences Europe* 28 (2016), No. 1, pp. 26. doi: 10.1186/s12302-016-0094-5
- Oltmanns, J.; Kaiser, E.; Heine, K.; Schneider, K.; Hesse, S.; Hahn, S. Effectiveness of personal protective equipment against dermal exposure – a comparative survey. 1st edition. Dortmund (Germany): Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, 2016, 199 pp. doi: 10.21934/baua:bericht20161101
- Pittiruti, M.; Sasse, M.; Braun, A.; Keck, C.; Lankers, M.; Munoz, P. G.; Ryder, M.; Stone, J. Time to rethink filtration. In: *British Journal of Nursing* 25 (2016), Suppl. 19, pp. 1-12. doi: 10.12968/bjon.2016.25.Sup19.1
- Prasse, A. The diagnosis, differential diagnosis, and treatment of sarcoidosis. In: *Deutsches Ärzteblatt international* 113 (2016), No. 33-34, pp. 565-74. doi: 10.3238/arztebl.2016.0565
- Przybylak, K. R.; Schultz, T. W.; Richarz, A.-N.; Mellor, C. L.; Escher, S. E.; Cronin, M. T. D. Read-across of 90-day rat oral repeated-dose toxicity: a case study for selected β -olefinic alcohols. In: *Computational Toxicology* (2016) [epub ahead of print]. doi: 10.1016/j.comtox.2016.11.001
- Schafer, C.; Goder, A.; Beyer, M.; Kiweler, N.; Mahendrarajah, N.; Rauch, A.; Nikolova, T.; Stojanovic, N.; Wiczorek, M.; Reich, T. R.; Tomicic, M. T.; Linnebacher, M.; Sonnemann, J.; Dietrich, S.; Sellmer, A.; Mahboobi, S.; Heinzl, T.; Schneider, G.; Kramer, O. H. Class I histone deacetylases regulate p53/NF- κ B crosstalk in cancer cells. In: *Cellular Signalling* 29 (2016), pp. 218-225. doi: 10.1016/j.cellsig.2016.11.002
- Schäfers, C.; Licht, O.; Bitsch, A. Endokrin wirksame Umweltchemikalien in Lebensmitteln. In: *Internistische Praxis* 57 (1), pp. 175-180.
- Schroder, K.; Escher, S. E.; Hoffmann-Dorr, S.; Kuhne, R.; Simetska, N.; Mangelsdorf, I. Evaluation of route-to-route extrapolation factors based on assessment of repeated-dose toxicity studies compiled in the database RepDose®. In: *Toxicology Letters* 261 (2016), pp. 32-40. doi: 10.1016/j.toxlet.2016.08.013
- Schuermann, G.; Ebert, R. U.; Tluczkiwicz, I.; Escher, S. E.; Kuhne, R. Inhalation threshold of toxicological concern (TTC) – structural alerts discriminate high from low repeated-dose inhalation toxicity. In: *Environment International* 88 (2016), pp. 123-132. doi: 10.1016/j.envint.2015.12.005
- Schüz, J.; Dasenbrock, C.; Ravazzani, P.; Roosli, M.; Schar, P.; Bounds, P. L.; Erdmann, F.; Borkhardt, A.; Cobaleda, C.; Fedrowitz, M.; Hamnerius, Y.; Sanchez-Garcia, I.; Seger, R.; Schmiegelow, K.; Ziegelberger, G.; Capstick, M.; Manser, M.; Muller, M.; Schmid, C. D.; Schürmann, D.; Struchen, B.; Kuster, N. Extremely low-frequency magnetic fields and risk of childhood leukemia: a risk assessment by the ARIMMORA consortium. In: *Bioelectromagnetics* 37 (2016), No. 3, pp. 183-189. doi: 10.1002/bem.21963
- Selich, A.; Daudert, J.; Hass, R.; Philipp, F.; von Kaisenberg, C.; Paul, G.; Cornils, K.; Fehse, B.; Rittinghausen, S.; Schambach, A.; Rothe, M. Massive clonal selection and transiently contributing clones during expansion of mesenchymal stem cell cultures revealed by lentiviral RGB-barcode technology. In: *Stem Cells Translational Medicine* 5 (2016), No. 5, pp. 591-601. doi: 10.5966/sctm.2015-0176
- Shrestha, P.; Junker, T.; Fenner, K.; Hahn, S.; Honti, M.; Bakkour, R.; Diaz, C.; Hennecke, D. Simulation studies to explore biodegradation in water-sediment systems: from OECD 308 to OECD 309. In: *Environmental Science & Technology* 50 (2016), No. 13, pp. 6856-6864. doi: 10.1021/acs.est.6b01095
- Subramanian, D. R.; Gupta, S.; Burggraf, D.; Vom Silberberg, S. J.; Heimbeck, I.; Heiss-Neumann, M. S.; Haeussinger, K.; Newby, C.; Hargadon, B.; Raj, V.; Singh, D.; Kolsum, U.; Hofer, T. P.; Al-Shair, K.; Luetzen, N.; Prasse, A.; Müller-Quernheim, J.; Benea, G.; Leprotti, S.; Boschetto, P.; Gorecka, D.; Nowinski, A.; Oniszh, K.; Castell, W. Z.; Hagen, M.; Barta, I.; Dome, B.; Strausz, J.; Greulich, T.; Vogelmeier, C.; Koczulla, A. R.; Gut, I.; Hohlfeld, J.; Welte, T.; Lavae-Mokhtari, M.; Ziegler-Heitbrock, L.; Brightling, C.; Parr, D. G. Emphysema- and airway-dominant COPD phenotypes defined by standardised quantitative computed tomography. In: *European Respiratory Journal* 48 (2016), No. 1, pp. 92-103. doi: 10.1183/13993003.01878-2015
- Suzuki, T.; Asami, M.; Hoffmann, M.; Lu, X.; Guzvic, M.; Klein, C. A.; Perry, A. C. Mice produced by mitotic reprogramming of sperm injected into haploid parthenogenotes. In: *Nature Communications* 7 (2016), p. 12676. doi: 10.1038/ncomms12676
- Temann, A.; Golovina, T.; Neuhaus, V.; Thompson, C.; Chichester, J. A.; Braun, A.; Yusibov, V. Evaluation of inflammatory and immune responses in long-term cultured human precision-cut lung slices. In: *Human Vaccines & Immunotherapeutics* (2016) [epub ahead of print]. doi: 10.1080/21645515.2017.1264794
- Tluczkiwicz, I.; Kuhne, R.; Ebert, R. U.; Batke, M.; Schuermann, G.; Mangelsdorf, I.; Escher, S. E. Inhalation TTC values: a new integrative grouping approach considering structural, toxicological and mechanistic features. In: *Regulatory Toxicology and Pharmacology* 78 (2016), pp. 8-23. doi: 10.1016/j.yrtph.2016.03.022
- Tran, D. D.; Koch, A.; Saran, S.; Armbrrecht, M.; Ewald, F.; Koch, M.; Wahlicht, T.; Wirth, D.; Braun, A.; Nashan, B.; Gaestel, M.; Tamura, T. Extracellular-signal regulated kinase (Erk1/2), mitogen-activated protein kinase-activated protein kinase 2 (MK2) and tristetraprolin (TTP) comprehensively regulate injury-induced immediate early gene (IEG) response in in-vitro liver organ culture. In: *Cellular Signalling* 28 (2016), No. 5, pp. 438-47. doi: 10.1016/j.cellsig.2016.02.007

Tsikis, D.; Kayacelebi, A. A.; Hanff, E.; Mitschke, A.; Beckmann, B.; Tillmann, H. C.; Gutzki, F. M.; Müller, M.; Bernasconi, C.
GC-MS and GC-MS/MS measurement of ibuprofen in 10-µL aliquots of human plasma and mice serum using [α-methyl-²H₃]ibuprofen after ethyl acetate extraction and pentafluorobenzyl bromide derivatization: discovery of a collision energy-dependent H/D isotope effect and pharmacokinetic application to inhaled ibuprofen-arginine in mice.
In: Journal of Chromatography B. Analytical Technologies in the Biomedical and Life Sciences (2016) [pub ahead of print].
doi: 10.1016/j.jchromb.2016.06.014

Uhde, A. K.; Herder, V.; Akram Khan, M.; Ciurkiewicz, M.; Schaudien, D.; Teich, R.; Floess, S.; Baumgartner, W.; Huehn, J.; Beineke, A.
Viral infection of the central nervous system exacerbates interleukin-10 receptor deficiency-mediated colitis in SJL mice.
In: PLOS ONE 11 (2016), No. 9, p. e0161883.
doi: 10.1371/journal.pone.0161883

Veith, N.; Ziehr, H.; MacLeod, R. A.; Reamon-Buettner, S. M.
Mechanisms underlying epigenetic and transcriptional heterogeneity in Chinese hamster ovary (CHO) cell lines.
In: BMC Biotechnology 16 (2016), Art. 6, 16 pp.
doi: 10.1186/s12896-016-0238-0

Waschki, B.; Kirsten, A. M.; Holz, O.; Meyer, T.; Lichtiginghagen, R.; Rabe, K. F.; Magnussen, H.; Welte, T.; Watz, H.; Janciauskiene, S.
Angiotensin-like protein 4 and cardiovascular function in COPD.
In: BMJ Open Respiratory Research 3 (2016), No. 1, p. e000161.
doi: 10.1136/bmjresp-2016-000161

Wiesner, J.; Ziemann, C.; Hintz, M.; Reichenberg, A.; Ortmann, R.; Schlitzer, M.; Fuhst, R.; Timmesfeld, N.; Vilcinskas, A.; Jomaa, H.
FR-900098, an antimalarial development candidate that inhibits the non-mevalonate isoprenoid biosynthesis pathway, shows no evidence of acute toxicity and genotoxicity.
In: Virulence 7 (2016), No. 6, pp. 718-28.
doi: 10.1080/21505594.2016.1195537

Wilson, S. J.; Ward, J. A.; Sousa, A. R.; Corfield, J.; Bansal, A. T.; De Meulder, B.; Lefaudeux, D.; Auffray, C.; Loza, M. J.; Baribaud, F.; Fitch, N.; Sterk, P. J.; Chung, K. F.; Gibeon, D.; Sun, K.; Guo, Y. K.; Adcock, I.; Djukanovic, R.; Dahlen, B.; Chanez, P.; Shaw, D.; Krug, N.; Hohlfeld, J.; Sandstrom, T.; Howarth, P. H.
Severe asthma exists despite suppressed tissue inflammation: findings of the U-BIOPRED study.
In: European Respiratory Journal 48 (2016), No. 5, pp. 1307-1319.
doi: 10.1183/13993003.01129-2016

Abstracts

Bitsch, A.; Batke, M.; Gundert-Remy, U.; Gütlein, M.; Kramer, S.; Partosch, F.; Seeland, M.
Optimizing clustering strategies for chemical categories: toxicological verification of derived clusters.
In: The Toxicologist 55 (2016), No. 1, p. 488, Abstract PS 3081.

Boge, L.; Häußler, S.; Knebel, J.; Müller, M.; Wronski, S.
Development of a co-culture system for inhalative therapeutics against *Pseudomonas aeruginosa* infections.
In: The Toxicologist 55 (2016), No. 1, p. 221, Abstract PS 1941.

Booth, J. L.; Duggan, E. S.; Patel, V. I.; Metcalf, J.; Langer, M.; Coggeshall, K. M.; Braun, A.
Alveolar escape by *Bacillus anthracis* spores does not require a carrier cell and is not altered by lethal toxin.
In: Journal of Investigative Medicine 64 (2016), No. 4, pp. 960-961.
doi: 10.1136/jim-2016-000120.101

Borlak, J.; Reamon Buettner, S.-M.
Epigenetic silencing of the lung tumor suppressor cell adhesion molecule 1.
In: Toxicology Letters 258 (2016), Suppl., p. S92.

Brinkman, P.; Wagener, A. H.; Hekking, P.-P.; Bansal, A. T.; Wang, Y.; Weda, H.; Knobel, H. H.; Vink, T. J.; Rattray, N. J.; D'Amico, A.; Pennazza, G.; Santonico, M.; Bakke, P. S.; Caruso, M.; Chung, K. F.; Corfield, J.; Dahlen, S.-E.; Djukanovic, R.; Geiser, T.; Horvath, I.; Krug, N.; Musial, J.; Shaw, D. E.; Pandis, I.; Sandstrom, T.; Sousa, A. R.; Montuschi, P.; Fowler, S. J.; Sterk, P. J.
Longitudinal replication of severe asthma exhaled breath phenotypes by the U-BIOPRED electronic nose platform.
In: American Journal of Respiratory and Critical Care Medicine 193 (2016), Abstract A4919.

Brodbeck, C.; Wolf, K.; Ritter, D.; Knebel, J.
Use of computational fluid dynamics for optimization of cell-based in vitro methods in inhalation research.
In: Toxicology Letters 258 (2016), Suppl., p. S141.

Buschmann, J.
Changes introduced with the new OECD 443 method and implications on the toxicological interpretation.
In: Toxicology Letters 258 (2016), Suppl., p. S52.

Creutzenberg, O.; Hansen, T.; Schuchardt, S.; Tillmann, T.; Knebel, J.
Method for identification of low soluble, biopersistent dusts (GBS).
In: The Toxicologist 55 (2016), No. 1, p. 119, Abstract PS 1510.

Creutzenberg, O.; Hansen, T.; Schuchardt, S.; Tillmann, T.; Knebel, J.
Method for identification of low soluble, biopersistent dusts (GBS).
In: Toxicology Letters 258 (2016), Suppl., pp. S197-S198.

Creutzenberg, O.; Hansen, T.; Schuchardt, S.; Tillmann, T.; Knebel, J.
Method for identification of low soluble, biopersistent dusts (GBS) – comparison of intratracheal installation and subacute inhalation.
In: Naunyn-Schmiedeberg's Archives of Pharmacology 389 (2016), Suppl. 1, p. S47, Abstract 189.
doi: 10.1007/s00210-015-1087-4

Curths, C.; Jimenez-Delgado, S.; Wichmann, J.; Kap, Y. S.; Kaup, F.-J.; Braun, A.; Sewald, K.; Knauf, S.; Dahlmann, F.
Marmoset monkeys as a model for human allergic asthma.
In: American Journal of Respiratory and Critical Care Medicine 193 (2016), Abstract A4919.

Danov, O.; Escher, S.; Schröder, K.; Koschmann, J.; Niehof, M.; Vorgrimmler, D.; Braubach, P.; Jonigk, D.; Hansen, T.; Braun, A.; Sewald, K.
Evaluation of chemically induced cytotoxicity of read across compounds in rat and human lung tissue.
In: The Toxicologist 55 (2016), No. 1, p. 402, Abstract PS 2710.

Ernst, H.; Ma-Hock, L.; Keller, J.; Groeters, S.; van Ravenzwaay, B.; Gebel, T.; Schaudien, D.; Rittinghausen, S.; Landsiedel, R.
Histopathological findings after 12 months inhalation to nanoceria.
In: Naunyn-Schmiedeberg's Archives of Pharmacology 389 (2016), Suppl. 1, p. S53, Abstract 219.
doi: 10.1007/s00210-015-1087-4

Escher, S.; Turek, C.; Campos, S.; Edwards, J.; Ferret, P.; Höfer, N.; Kosemund, K.; Schnabel, J.; Van Ravenzwaay, B.; Hollnagel, H. M.
Thresholds of toxicological concern – overview of ongoing scientific developments.
In: Toxicology Letters 258 (2016), Suppl., p. S58, Abstract OSC02-003.

Escher, S. E.; Pastor, M.; Carrio, P.; Hoffmann-Doerr, S.; Steger-Hartmann, T.; Mangelsdorf, I.
Time extrapolation factors for risk assessment: are group-specific extrapolation factors possible?
In: The Toxicologist 55 (2016), No. 1, p. 396, Abstract PS 2684.

Farcial, L.; Ziemann, C.; Oliveira, H.; Burla, S.; Creutzenberg, O.
In-vitro and in-vivo investigations to obtain validated toxicity data of graphene nanoplatelets.
In: Toxicology Letters 258 (2016), Suppl., p. S261.

Fenner, K.; Honti, M.; Junker, T.; Shrestha, P.; Hahn, S.; Matthies, M.; Hennecke, D.
Identifying limitations of the OECD water-sediment test (OECD 308) and developing suitable alternatives to assess persistence.
In: SETAC Europe 26th Annual Meeting Abstract Book (2016), p. 108, Abstract 478.

Granitzny, A.; Knebel, J.; Dasenbrock, C.; Steinberg, P.; Hansen, T.
In-vitro models for the prediction of idiosyncratic drug-induced liver injury.
In: The Toxicologist 55 (2016), No. 1, p. 239, Abstract PS 2016.

Granitzny, A.; Knebel, J. W.; Steinberg, P.; Dasenbrock, C.; Hansen, T.
Prediction of idiosyncratic drug-induced hepatotoxicity: pro-inflammatory stimuli are needed to differentiate between iDILI and non-DILI compounds.
In: Naunyn-Schmiedeberg's Archives of Pharmacology 389 (2016), Suppl. 1, p. S91, Abstract 386.
doi: 10.1007/s00210-015-1087-4

Haider, G.; Wiegand, S.; Spies, E.; Braun, A.; Kummer, W.; Nassenstein, C.
Effects of TRPA1 agonists on murine airways.
In: Pneumologie 70 (2016), No. 7, Abstract P46.
doi: 10.1055/s-0036-1584649

Hesse, C.; Mang, S.; Hoymann, H.-G.; Niehof, M.; Braubach, P.; Jonigk, D.; Warnecke, G.; Pfennig, O.; Fieguth, H.-G.; Braun, A.; Sewald, K.
Induction of pro-fibrotic biomarkers in precision-cut lung slices (PCLS).
In: European Respiratory Journal 48 (2016), Suppl. 60, OA479.
doi: 10.1183/13993003.congress-2016.OA479

Hesse, C.; Mang, S.; Niehof, M.; Hoymann, H.-G.; Braubach, P.; Jonigk, D.; Warnecke, G.; Pfennig, O.; Fieguth, H.-G.; Braun, A.; Sewald, K.
Identification of pro-fibrotic biomarkers in precision-cut lung slices (PCLS).
In: ALTEX Proceedings 5 (2016), No. 1, p. 90.

- Hesse, S.; Blümlein, K.; Hahn, S.
Describing the effectiveness of sector-specific exposure controls.
In: ISES 2016 Abstract Book (2016), p. 24, Abstract Mo-Sy-B1.2.
- Hesse, S.; Hahn, S.; Lamb, J.; Tongeren, M. v.
Conceptual evaluation and uncertainty of Tier 1 exposure assessment models used under REACH.
In: ISES 2016 Abstract Book (2016), p. 644, Abstract We-SY-B3.3.
- Hohlfeld, J.; Biller, H.; Hagedorn, I.; Berliner, D.; Bauersachs, J.; Welte, T.; Vogel-Claussen, J.
Ein neuartiges Studiendesign mit Magnetresonanztomographie-Bildgebungsverfahren zur Untersuchung des Effekts der Indacaterol/Glycopyrronium-Fixdosiskombination auf die kardiale Funktion bei COPD-Patienten: die CLAIM-Studie.
In: *Pneumologie* 70 (2016), Abstract P62.
doi: 10.1055/s-0036-1572020
- Holz, O.; Allers, M.; Gaida, A.; Schuchardt, S.; Hohlfeld, J. M.; Zimmermann, S.
Comparison of COPD-related breath VOCs assessed by a compact high-resolution closed-loop GC-IMS and by standard GC-MS.
In: *American Journal of Respiratory and Critical Care Medicine* 193 (2016), Abstract A14234.
- Holz, O.; Gaida, A.; Nell, C.; Allers, M.; Schuchardt, S.; Zimmermann, S.; Koczulla, R.; Hohlfeld, J. M.
Rating the value of COPD-related breath VOCs in models created by linear discriminant analysis.
In: *American Journal of Respiratory and Critical Care Medicine* 193 (2016), Abstract A4919.
- Holz, O.; Heusser, K.; Gaida, A.; Allers, M.; Zimmermann, S.; Müller, M.; Schuchardt, S.; Schindler, C.; Tank, J.; Jordan, J.; Hohlfeld, J. M.
Inflammatory response to the exposure with ultra-fine particles and ozone.
In: *European Respiratory Journal* 48 (2016), Suppl. 60, Abstract PA1836.
doi: 10.1183/13993003.congress-2016.PA1836
- Hoymann, H. G.; Schaudien, D.; Hansen, T.; Niehof, M.; Braun, A.
Functional, histological and biochemical endpoints for assessing antifibrotic efficacy in a rat model of pulmonary fibrosis.
In: *American Journal of Respiratory and Critical Care Medicine* 193 (2016), Abstract A4172.
- Jiménez-Delgado, S. M.; Obernolte, H.; Hobbie, S.; Schindler, S.; Jonigk, D.; Warnecke, G.; Braubach, P.; Bersch, C.; Pfennig, O.; Fieguth, H.-G.; Sewald, K.; Braun, A.
Transient receptor potential (TRP) ion channels activation in vital human precision-cut lung slices lead to bronchoconstriction and is neuropeptide substance p-dependent.
In: *American Journal of Respiratory and Critical Care Medicine* 193 (2016), Abstract A1342.
- Kodandaraman, G.; Rahmer, H.; Gómez, J.; Schaudien, D.; Brockmeyer, H.; Voepel, I.; Westendorf, A.; Creutzenberg, O.; Ziemann, C.
The PHOENIX project: nano-layered hybrid particles as flame retardant additives – toxicological in-vitro investigations using lung-relevant cell models.
In: *Naunyn-Schmiedeberg's Archives of Pharmacology* 389 (2016), Suppl. 1, p. S53, Abstract 218.
doi: 10.1007/s00210-015-1087-4
- Konzok, S.; Braubach, P.; Peter, D.; Jonigk, D.; Fieguth, H.-G.; Braun, A.; Sewald, K.
Different pathways of inflammasome activation in human precision-cut lung slices (PCLS).
In: *American Journal of Respiratory and Critical Care Medicine* 193 (2016), Abstract A1425.
- Konzok, S.; Dehmel, S.; Braubach, P.; Jonigk, D.; Pfennig, O.; Fieguth, H.-G.; Braun, A.; Sewald, K.
Anti-cancer effects of bevacizumab and cisplatin on cancer cell-invaded human ex-vivo lung tissue.
In: *European Respiratory Journal* 48 (2016), Suppl. 60, OA6022.
doi: 10.1183/13993003.congress-2016.OA6022
- Ma-Hock, L.; Ernst, H.; Gröters, S.; Rittinghausen, S.; Keller, J.; van Ravenzwaay, B.; Schaudien, D.; Landsiedel, R.
Histopathological findings after 12 months inhalation to nanoceria.
In: *The Toxicologist* 55 (2016), No. 1, p. 362, Abstract PL 2537.
- Merten, C. G.; Oltmanns, J.; Bohlen, M.-L.; Escher, S.; Licht, O.; Macleod, M.; Silano, V.; Georgiadis, N.; Kass, G.
Testing a procedure for the identification of emerging chemical risks in the food chain.
In: ISES 2016 Abstract Book (2016), p. 493, Abstract Tu-Po-28.
- Metcalfe, J. P.; Booth, J. L.; Duggan, E. S.; Patel, V. I.; Langer, M.; Braun, A.; Coggeshall, K. M.
Bacillus anthracis spore movement and uptake by cells resident in the human lung are not affected by anthrax lethal toxin.
In: *American Journal of Respiratory and Critical Care Medicine* 193 (2016), Abstract A5479.
- Obernolte, H.; Braubach, P.; Jonigk, D.; Pfennig, O.; Fieguth, H.-G.; Braun, A.; Wronski, S.; Sewald, K.
Responses to rhinovirus infection in human lung slices are reduced by rupintrivir.
In: *European Respiratory Journal* 48 (2016), Suppl. 60, Abstract PA3646.
doi: 10.1183/13993003.congress-2016.PA3646
- Obernolte, H.; Ritter, D.; Knebel, J. W.; Braubach, P.; Jonigk, D.; Fieguth, H.-G.; Braun, A.; Sewald, K.
Cigarette smoke and cigarette smoke condensate induce early biomarkers of inflammation and cytotoxicity in precision-cut lung slices.
In: *American Journal of Respiratory and Critical Care Medicine* 193 (2016), Abstract A14257.
- Obernolte, H.; Ritter, D.; Knebel, J.; Braubach, P.; Jonigk, D.; Warnecke, G.; Krüger, M.; Fieguth, H. G.; Pfennig, O.; Braun, A.; Sewald, K.
Cigarette smoke and cigarette smoke condensate induce inflammation and cytotoxicity in precision-cut lung slices (PCLS).
In: *Pneumologie* 70 (2016), No. 7, Abstract P42.
doi: 10.1055/s-0036-1584649
- Reamon-Buettner, S. M.; Hiemisch, A.; Voepel, I.; Ziemann, C.
Detection of transcriptomic signature for a senescence-associated secretory phenotype (SASP) in human peritoneal mesothelial cells exposed to multiwalled carbon nanotubes.
In: *The Toxicologist* 55 (2016), No. 1, p. 583, Abstract PS 583.
- Reamon-Buettner, S. M.; Hiemisch, A.; Voepel, I.; Ziemann, C.
Transcriptome signatures in human peritoneal mesothelial cells after exposure to multiwalled carbon nanotubes support a potential role of cellular senescence in mesothelioma development.
In: *Naunyn-Schmiedeberg's Archives of Pharmacology* 389 (2016), Suppl. 1, p. S52, Abstract 214.
doi: 10.1007/s00210-015-1087-4
- Requardt, H.; Hansen, T.; Hampel, S.; Steinberg, P.; Dasenbrock, C.
Investigating the cytotoxicity of different forms of multi-walled carbon nanotubes and their use as a potential drug delivery carrier.
In: *Naunyn-Schmiedeberg's Archives of Pharmacology* 389 (2016), Suppl. 1, p. S53, Abstract 216.
doi: 10.1007/s00210-015-1087-4
- Ritter, D.; Bitsch, A.; Elend, M.; Schuchardt, S.; Hansen, T.; Brodbeck, C.; Knebel, J.; Fautz, R.; Fuchs, A.; Gronewold, C.
Development of an experimental cell-based approach to evaluate biological effects of aerosols from the application of hair-straightening products in vitro using relevant product application and cell exposure conditions.
In: *The Toxicologist* 55 (2016), No. 1, p. 598, Abstract PS 3548.
- Ritter, D.; Knebel, J.; Wronski, S.; Montes, A.; Niehof, M.
Development of an in-vitro testing platform for aerosols containing inhalable antibiotic active compounds as a part of the EU project "PneumoNP".
In: *Toxicology Letters* 258 (2016), Suppl., p. S146.
- Schaudien, D.; Hackbarth, A.; Ernst, H.; Rittinghausen, S.; Leonhardt, A.; Heinrich, H.; Creutzenberg, O.
No immunohistologically detectable genotoxicity or proliferation following 90-day inhalation of multi-walled carbon nanotubes.
In: *The Toxicologist* 55 (2016), No. 1, p. 587, Abstract PS 3499.
- Schmeink, S.; Bitsch, A.; Genth, H.
Analysis of selected substances from the SkinAb database.
In: *Naunyn-Schmiedeberg's Archives of Pharmacology* 389 (2016), Suppl. 1, p. S89, Abstract 375.
doi: 10.1007/s00210-015-1087-4
- Schwotzer, D.; Niehof, M.; Hansen, T.; Schuchardt, S.; Tillmann, T.; Ernst, H.; Creutzenberg, O.
Investigation of CeO₂ nanoparticle toxicity in a 90-day inhalation test.
In: *The Toxicologist* 55 (2016), No. 1, p. 363, Abstract PL 2542.
- Schwotzer, D.; Niehof, M.; Hansen, T.; Schuchardt, S.; Tillmann, T.; Ernst, H.; Creutzenberg, O.
Toxicity of CeO₂ nanoparticles estimated in a 90-day nose-only inhalation study.
In: *Naunyn-Schmiedeberg's Archives of Pharmacology* 389 (2016), Suppl. 1, p. S51, Abstract 210.
doi: 10.1007/s00210-015-1087-4
- Schwotzer, D.; Niehof, M.; Hansen, T.; Tillmann, T.; Ernst, H.; Creutzenberg, O.
Toxicity of cerium dioxide nanoparticles – effects from a 90-day inhalation study.
In: *Toxicology Letters* 258 (2016), Suppl., p. S55.
- Sundarasetty, B. S.; Schneider, A.; Sewald, K.; Rittinghausen, S.; Braun, A.; Figueiredo, C.; Ganser, A.; Striepecke, R.
No GVHD, but human inflammatory "cytokine storm" and mouse macrophage activation upon accelerated development of human CD4⁺ effector memory T cells in long-term humanized mice.
In: *Molecular Therapy* 24 (2016), Suppl. 1, p. S188, Abstract 476.

Tluczkiewicz, I.; Batke, M.; Webb, S. J.; Garcia-Sterna, R.; Bento, P.; Escher, S. E. Analysis of the potential of chemicals to induce anemia based on compound-specific properties. In: *The Toxicologist* 55 (2016), No. 1, p. 387, Abstract PL 2650.

Volk, J.; Leyhausen, G.; Geurtsen, W.; Ziemann, C. Camphorquinone-induced oxidative stress and mutations in L5178y tk⁺ mouse lymphoma cells. In: *Journal of International Society of Antioxidants in Nutrition & Health* 3 (2016), No. 3, Abstract 1245. doi: 10.18143/JISANH_v3i3_1245

Waschki, B.; Kirsten, A.; Holz, O.; Meyer, T.; Lichtinghagen, R.; Rabe, K.; Magnussen, H.; Welte, T.; Watz, H.; Janciauskiene, S. Association of angiotensin-like protein 4 with cardiovascular function in patients with COPD. In: *European Respiratory Journal* 48 (2016), Suppl. 60, OA3004. doi: 10.1183/13993003.congress-2016.OA3004

Waschki, B.; Kirsten, A.-M.; Holz, O.; Meyer, T.; Lichtinghagen, R.; Rabe, K. F.; Braubach, P.; Kaup, F.-J.; Braun, A.; Eggel, A.; Dahlmann, F.; Sewald, K.; Knauf, S. α 1-Antitrypsin (A1AT) serum levels as marker of systemic inflammation in non-A1AT-deficient patients with COPD. In: *American Journal of Respiratory and Critical Care Medicine* 193 (2016), Abstract A3488.

Wichmann, J.; Jimenez-Delgado, S.; Curths, C.; Schmitt, A.; Dunker, S.; Jonigk, D.; Fioravanzo, E.; Kaup, F.-J.; Braun, A.; Eggel, A.; Dahlmann, F.; Sewald, K.; Knauf, S. Efficacy assessment of a novel disruptive IgE inhibitor in non-human primate and human precision-cut lung slices. In: *American Journal of Respiratory and Critical Care Medicine* 193 (2016), Abstract A6684.

Yang, C.; Arvidson, K.; Cheeseman, M.; Cronin, M.; Enoch, S.; Escher, S.; Fioravanzo, E.; Jacobs, K.; Steger-Hartmann, T.; Tluczkiewicz, I.; Tarkhov, A.; Rathman, J.; Vitcheva, V.; Mostrag, A.; Worth, A. Development of a master database of non-cancer threshold of toxicological concern and potency categorization based on ToxPrint chemotypes. In: *The Toxicologist* 55 (2016), No. 1, p. 273, Abstract PS 2163.

Theses

Doctoral theses

Feliciello, Giancarlo

Identification of translocations in single disseminated cancer cells. University of Regensburg, 2016

Prenzler, Frauke

Quantification of allergic processes in the lung. Hannover Medical School, 2016

Walter, Dorothee

An alternative model for efficacy testing of exogenous surfactant using the isolated perfused rat lung (IPL). University of Veterinary Medicine Hannover, 2016

Wang-Lauenstein, Lan

Assessment of chemical-induced local irritation and inflammation in organotypic lung tissue model – PCLS. Leibniz Universität Hannover, 2016

Wichmann, Judy

Untersuchungen zur Prävention von Asthma in einem Ex-vivo-Lungenmodell unter Verwendung nicht-menschlicher Primaten. University of Veterinary Medicine Hannover, 2016

Master theses

Detzer, Julia

Evaluation of inflammatory markers induced by exogenous noxae in a human pulmonary co-culture in-vitro system. Hannover Medical School, 2016

Kodandaraman, Geema

Comparative assessment of the (geno)toxic potential of certain (nano)materials, intended to be used as flame retardant additives, using lung-relevant cell models. University of Duisburg-Essen, 2016

Kuhn, Anna

Adaptation and evaluation of genomic sequence analysis of reads resulting from recurrent stochastic concatenation of MseI fragments of a single cell equivalent. University of Regensburg, 2015

Laßwitz, Lisa

Effect of rhinovirus infection on asthma phenotype ex vivo. Hannover Medical School, 2016

Schulz, Laura

Charakterisierung von funktionell immortalisierten humanen Lungenepithelzellen zur Etablierung eines In-vitro-Modells für die toxikologische Untersuchung von luftgetragenen Substanzen. RWTH Aachen, 2016

Volkwein, Annika

Effect of viral infection on asthma phenotype in precision-cut lung slices. University of Veterinary Medicine Hannover, 2016

Winterberg, Dorothee

Induktion von profibrotischen Signalwegen in Ex-vivo-Gewebeschnitten der Lunge. Hannover Medical School, 2016

Bachelor theses

Ganiyu-Noibi, Athina

The impact of EpCAM on proliferation and migration of prostate cancer cells. University of Regensburg, 2016

Möller, Marit

Weiterentwicklung einer API-Produktionsplattform: Generierung einer scFv-produzierenden CHO-Zelllinie und Optimierung der Methodik. Technische Universität Braunschweig, 2016

Seifert, Bastian

Datenbank für toxikologische In-vitro-Assays: Strukturdesign, Datenaufarbeitung und -analyse. University of Applied Sciences Emden/Leer, 2016

Invited lectures

Dr. Philipp Badorrek

Feasibility in recruitment – views from the sponsor and the investigator. PCMG Annual Conference 2016 Rome (Italy), June 10, 2016

Dr. Annette Bitsch

Praktische Erfahrungen mit Datenanforderungen für das Biozid-Produktossier. Seminar "Erfahrungen mit der Umsetzung der Biozidprodukteverordnung (BPR) EU 528/2012" Biocity, Leipzig (Germany), June 2, 2016

Development of in-vitro test methods. Conference of Applied Hygiene, Microbiology and Virology Hamburg (Germany), October 6-7, 2016

Prof. Dr. Armin Braun

Mechanistic aspects of sensitization. Workshop "Dermal exposure and diisocyanates: current knowledge and research needs". International Isocyanate Institute, Inc. (III) Düsseldorf (Germany), May 10, 2016

Use of precision-cut lung slices for pharmacological research. Stanford University San Francisco, California (USA), May 16, 2016

Particle and endotoxin effects. Satellite symposium "New understandings in IV filtration relevant to patient care", World Congress on Vascular Access Lisbon (Portugal), June 24, 2016

In-vivo and ex-vivo models of respiratory infection and exacerbation. Robert Koch Institute Wernigerode (Germany), September 1, 2016

Nerven und Immunzellen: Duo infernale der Allergie? 11th German Allergy Congress Berlin, September 29, 2016

Bringing innovative therapies into the clinic considering a highly regulated environment. Colloquium of the REBIRTH cluster of excellence Hannover (Germany), November 9, 2016

Dr. Jochen Buschmann

GMO and glyphosate: Teratology Society and European Teratology Society Exchange Lecture.

Teratology Society 56th Annual Meeting
San Antonio, Texas (USA), June 26-29, 2016
and

44th Annual Meeting of the European Teratology Society
Dublin (Ireland), September 11-14, 2016

Changes introduced with the new EOGRTS method and implications on the toxicological interpretation

52nd Congress of the European Societies of Toxicology (EUROTOX)
Seville (Spain), September 4-7, 2016

Dr. Otto Creutzenberg

Inhalt90: 90-day inhalation toxicity test with CeO₂ nanoparticles including gene expression analysis.

30th Meeting of the DECHEMA/VC Working Group "Responsible Production and Use of Nanomaterials"
Frankfurt/Main (Germany), April 20, 2016

Dr. Ilona Fleischhauer

Quality Management at Clinical Research Center (CRC) Hannover: concepts and experiences in early-phase clinical trials.

AGAH Workshop "Quality Management in Early-Phase Clinical Pharmacology Units"
Bonn (Germany), November 3, 2016

Dipl.-Dok. (FH) Martina Heina

Validierung computergestützter Systeme (CS): Vorgehensweisen am Fraunhofer ITEM.

Working committee on quality management "Qualitätsmanagement im VLS" in the Fraunhofer Group for Life Sciences
Hannover (Germany), June 17, 2016

Erfahrungen aus dem Projekt "Auswahl eines eDMS für das Fraunhofer ITEM".

Working committee on quality management "Qualitätsmanagement im VLS" in the Fraunhofer Group for Life Sciences
Leipzig (Germany), December 2, 2016

Prof. Dr. Dr. Uwe Heinrich

From NOAEC of the rat to NOAEC for humans.

Symposium "Granular Biopersistent Dust and Translational Toxicology: Deriving HECs/Occupational Limit Values", organized by the German Research Foundation's Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, BDI, The Voice of German Industry, the German Federal Ministry of Labor and Social Affairs, and the German Federal Institute for Occupational Safety and Health.
Berlin (Germany), December 8, 2016

Prof. Dr. Jens Hohlfeld

Surfactant – Bedeutung bei Lungenerkrankungen des Erwachsenen.

57th Annual Congress of the German Respiratory Society (DGP)
Leipzig (Germany), March 3, 2016

Clinical challenge models in airway diseases (asthma, allergic rhinitis, COPD) – lessons learned and future perspectives.

AstraZeneca seminar on experimental respiratory studies at Fraunhofer Mölndal (Sweden), December 15, 2016

Dr. Rupert Kellner

Technical background and structure of the DevTox website with practical comments on the use of this tool.

Annual conference of the Shanghai Society of Environmental Mutagens
Shanghai (China), November 1, 2016

Dr. Stefan Kirsch

Combined high-resolution single-cell genome and transcriptome analysis of disseminated cancer cells.

2nd International Symposium on Microgenomics
Paris (France), June 3, 2016

Prof. Dr. Christoph Klein

Selection and adaption during metastatic cancer progression.

University Hospital of Würzburg Department of Dermatology, Venerology and Allergology
Würzburg (Germany), June 15, 2016

Single-cell analysis and clinical adaptation and research.

DEPArray™ User Conference of Menarini-Silicon Biosystems
Bologna (Italy), October 25, 2016

Mechanism of early cancer spread.

Fondazione IRCCS Istituto Nazionale dei Tumori
Milan (Italy), December 2, 2016

Prof. Dr. Wolfgang Koch

Feinstaub in der Umwelt.

Elbcampus Hamburg-Harburg, Hamburg (Germany), November 30, 2016

Dr. Gustav Könnecker

Europäische Chemikalienagentur (ECHA) – aktuelle Entwicklungen im Kontext von REACH und CLP.

IPT REACH working committee, Federal Office of Bundeswehr Equipment, Information Technology and In-Service Support (BAAINBw)
Koblenz (Germany), September 14, 2016

Stoffregistrierung von der Datenlückenanalyse bis zur erfolgreichen REACH-Registrierung.

REACH – eine Herausforderung für die Wehrtechnik. Carl-Cranz-Gesellschaft e.V., Gesellschaft für technisch-wissenschaftliche Weiterbildung, Fraunhofer Institute for Chemical Technology ICT
Pfinztal/Karlsruhe (Germany), October 18-19, 2016

Prof. Dr. Norbert Krug

Early-phase proof-of-concept studies – the Fraunhofer perspective.

Workshop "Strategies in modern therapy research – a prerequisite for efficient translational medicine" at the Hannover Medical School
Hannover (Germany), February 25, 2016

U-BIOPRED: Bessere Asthma-Therapie mit Handprints?

57th Annual Congress of the German Respiratory Society (DGP)
Leipzig (Germany), March 5, 2016

Experience with pharmacodynamics challenge models in early-phase clinical trials: allergens, endotoxin, rhinovirus, ozone, hypoxia.

CIIM Focus Seminar "Cellular Therapies, Vaccines and Human Challenge Models"
Hannover (Germany), April 25, 2016

Exacerbation of obstructive lung disease.

International Congress of the European Respiratory Society
London (UK), September 3-7, 2016

Karriereförderung und Karrierestrukturen aus der Sicht der Fraunhofer-Gesellschaft.

Symposium "Clinician Scientist – Karriereförderung und -strukturen" of the Integrated Research and Treatment Centers (IFBs)
Hannover (Germany), October 24-25, 2016

Dr. Oliver Licht

REACH in Forschung und Entwicklung: Worauf ist zu achten?

39th Meeting of the working committee "Richtlinien-konformes Design für WEEE/RoHS/EuP"
Berlin (Germany), November 22, 2016

Toxikologische Datenanforderungen unter REACH.

REACH – eine Herausforderung für die Wehrtechnik. Carl-Cranz-Gesellschaft e.V., Gesellschaft für technisch-wissenschaftliche Weiterbildung, Fraunhofer Institute for Chemical Technology ICT
Pfinztal/Karlsruhe (Germany), October 18-19, 2016

May 2018: third and final registration deadline under REACH – importance for cosmetic ingredients.

Regulatory workshop "Worldwide legislation on cosmetic ingredients used in consumer products: legislation for cosmetic ingredients – the Americas and Europe", in-cosmetics 2016
Paris (France), April 12, 2016

Prof. Dr. Antje Prasse

Läuse und Flöhe: IPF und Lungenkrebs.

German Respiratory Society (DGP)
Leipzig (Germany), March 24, 2016

Antazida bei jedem Patienten -pro-.

German Respiratory Society (DGP)
Leipzig (Germany), March 24, 2016

Lungenfibrose – früh behandeln.

German Society of Internal Medicine (DGIM)
Mannheim (Germany), April 12, 2016

No need for biopsy: BAL predicts outcome and unravels new mechanisms.

International Conference of the American Thoracic Society
San Francisco, California (USA), May 18, 2016

Pathogenesis of idiopathic pulmonary fibrosis.

International Congress of the World Association for Sarcoidosis and other Granulomatous Disorders (WASOG) 2016
Gdansk (Poland), June 3, 2016

Therapie der Lungenfibrose.

Hannover Herz Lungen Messe
Hannover (Germany), June 4, 2016

ERS Update Lungenfibrose.

Expertenforum Hannover
Hannover (Germany), September 12, 2016

Airway basal cells of patients with IPF are epigenetically reprogrammed and promote fibrosis.

International Colloquium of Lung and Airway Fibrosis (ICLAF)
Dublin (Ireland), September 25, 2016

Kortikosteroide und was noch?

41st Annual Congress of the Northern German Society of Respiratory Medicine
Hamburg (Germany), November 4, 2016

Neue Aspekte zur Pathogenese der Lungenfibrose.
Expertenforum Halle
Halle (Germany), November 5, 2016

Die akute Exazerbation der Lungenfibrose.
Hannover Medical School/DZL BREATH "Hot Christmas Topic"
December 14, 2016

Dr. Katherina Sewald

Entwicklung eines Modells mit humanem Lungenmaterial für die Krebsforschung.
Pharmaceutical colloquium at Kiel University
Kiel (Germany), July 4, 2016

Dr. Henning Weigt

Drug development at the interface between academia and industry – a Fraunhofer perspective.
9th International VPM Days: "Translational Medicine: From Bug to Drug"
Hannover (Germany), September 15, 2016

Dipl.-Ing. Ariane Zwitscher

Requirements for the toxicological part of a BPR dossier, PT 1-5.
Conference of Applied Hygiene, Microbiology and Virology 2016
Hamburg, October 6-7, 2016

Contributions to congresses and conferences

Bluemlein, K.; Hesse, S.

Solvent transfer – effectiveness of selected risk management measures (RMMs) on airborne solvent exposure.
OH 2016 – Annual Conference of the British Occupational Hygiene Society
Glasgow (UK), April 25-28, 2016

Boge, L.; Pankalla, J.; Müller, M.; Knebel, J.; Wronski, S.

Development of in-vitro test systems for inhalation treatment of persistent *P. aeruginosa* lung infection.
15th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 21-22, 2016

Curths, C.; Jimenez-Delgado, S.; Wichmann, J.; Kap, Y. S.; Kaup, F.-J.; Braun, A.; Sewald, K.; Knauf, S.; Dahlmann, F.

A novel model for human allergic asthma in marmoset monkeys.
5th DZL Annual Meeting
Hannover (Germany), February 1-2, 2016

Curths, C.; Wichmann, J.; Jimenez-Delgado, S.; Kap, Y. S.; Knauf, Y.; Kaup, F.-J.; Braun, A.; Sewald, K.; Knauf, S.; Dahlmann, F.

Modeling features of human asthma in marmoset monkeys.
15th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 21-22, 2016

Czyż, Z. T.; Kirsch, S.; Lahmann, U.; Gužvić, M.; Feliciello, G.; Polzer, B.; Klein, C. A.

High-resolution parallel analysis of genome and transcriptome of single disseminated prostate cancer cells.
American Association for Cancer Research (AACR) Annual Meeting 2016
New Orleans, Louisiana (USA), April 16-20, 2016

Danov, O.; Sewald, K.; Creutzenberg, O.; Knebel, J.; Hansen, T.

Effects of carbon black nanoparticles on human cells and tissue explants.
NanoCare Cluster Meeting
Frankfurt/Main (Germany), May 3-4, 2016

Danov, O.; Volkwein, A.; Laßwitz, L.; Romberg, S.; Obernolte, H.; Braun, A.; Wronski, S.; Sewald, K.

Ex-vivo infection with rhinovirus in mouse precision-cut lung slices.
20th European Congress on Alternatives to Animal Testing
Linz (Austria), August 24-27, 2016

Danov, O.; Volkwein, A.; Romberg, S.; Obernolte, H.; Braun, A.; Wronski, S.; Sewald, K.

Comparison of rhinovirus infection with HRV1B to poly I:C in mouse precision-cut lung slices.
15th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 21-22, 2016

Danov, O.; Volkwein, A.; Romberg, S.; Obernolte, H.; Braun, A.; Wronski, S.; Sewald, K.

Respiratory viral infection of HRV1B in mouse precision-cut lung slices.
5th DZL Annual Meeting
Hannover (Germany), February 1-2, 2016

Ernst, H.; Ma-Hock, L.; Keller, J.; Gröters, S.; van Ravenzwaay, B.; Gebel, T.; Schaudien, D.; Rittinghausen, S.; Landsiedel, R.

Histopathological findings after 12-month inhalation of nanoceria.
82nd Annual Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology (DGPT)
Berlin (Germany), February 29-March 3, 2016

Farcal, L.; Ziemann, C.; Oliveira, H.; Burla, S.; Creutzenberg, O.

In-vitro and in-vivo investigations to obtain validated toxicity data of graphene nanoplatelets.
52nd European Congress of the European Societies of Toxicology
Seville (Spain), September 4-7, 2016

Granitzny, A.; Knebel, J.; Braun, A.; Steinberg, P.; Dasenbrock, C.; Hansen, T.

Extensive characterization of rat precision-cut liver slices by various viability and functional parameters during 24h culture.
ESTIV 2016 – International Congress of the European Society of Toxicology In Vitro (ESTIV)
Juan-Les-Pins (France), October 17-20, 2016

Granitzny, A.; Knebel, J.; Müller, M.; Braun, A.; Steinberg, P.; Dasenbrock, C.; Hansen, T.

Characterization of PMA-differentiated THP-1 cells for the use in transwell co-culture systems and the successful application in a hepatocyte-NPC model for the prediction of iDILI.

ESTIV 2016 – International Congress of the European Society of Toxicology In Vitro (ESTIV)
Juan-Les-Pins (France), October 17-20, 2016

Haider, G.; Sauer, A. L.; Wiegand, S.; Spies, E.; Hoymann, G.; Kummer, W.; Braun, A.; Nassenstein, C.

TRPA1, a cool receptor as a hot therapeutic target in asthma?
5th DZL Annual Meeting
Hannover (Germany), February 1-2, 2016

Heath, H.; Holz, O.; Stein, F.; Hohlfeld, J.; Mall, M.; Schultz, C.

Application of small molecule FRET reporters of proteolytic activity in a study of acute lung inflammation.
5th DZL Annual Meeting
Hannover (Germany), February 1-2, 2016

Hesse, C.; Mang, S.; Sender, S.; Hoymann, H.-G.; Niehof, M.; Braubach, P.; Jonigk, D.; Warnecke, G.; Pfennig, O.; Fieguth, H.-G.; Braun, A.; Sewald, K.

Ex-vivo induction of features displaying early onset pulmonary fibrosis in PCLS.
5th DZL Annual Meeting
Hannover (Germany), February 1-2, 2016

Hesse, S.; Hahn, S.; Bitsch, A.; Oltmanns, J.; Kaiser, E.; Heine, K.; Schneider, K.; Tischer, M.; Roitzsch, M.; Krause, M.

Comparative research of measurement methods used to quantify the effectiveness of personal protective equipment against dermal exposure.
7th OEESC – Occupational and Environmental Exposure of Skin to Chemicals Conference
Manchester (UK), September 19-21, 2016

Hoffmann, M.; Galle, J.

Stochastic system identification without a model – exploring feasible cell regulation types using piecewise linear functions and different experimental data.
International Conference of Systems Biology 2016
Barcelona (Spain), September 16-20, 2016

Hoffmann, M.; Scheitler, S.; Hodak, I.; Ulmer, A.; Klein, C. A.

Modeling cellular evolution during lymph node colonization in melanoma patients.
International Conference of Systems Biology 2016
Barcelona (Spain), September 16-20, 2016

Hohlfeld, J. M.

Wirksamkeitsprüfung von Medikamenten im Allergenprovokationsraum.
Expertenforum Allergologie
Hannover (Germany), April 15, 2016

Holz, O.

Breath volatile organic compounds in COPD.
15th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 21-22, 2016

Holz, O.; Gaida, A.; Lavae-Mokhtari, B.; Kruse, L.; Schuchardt, S.; Hohlfeld, J. M.

Comparison of breath VOC levels between two COPD studies.
IABR Breath Summit 2016
Zurich (Switzerland), September 14-16, 2016

Igl, B.-W.; Bitsch, A.; Bringezu, F.; Chang, S.; Dammann, M.; Froetschl, R.; Harm, V.; Kellner, R.; Krzykalla, V.; Poth, A.; Queisser, N.; Sutter, A.; Vonk, R.; Zeller, A.; Zellner, D.; Ziemann, C.

The GUM Working Group "Statistics": An interdisciplinary collaboration to evaluate and update statistical strategies in genotoxicity testing.
29th Annual Meeting of the German Society for Environmental Mutation Research (GUM)
Munich (Germany), October 12-14, 2016

- Kirsch, S.; Lahrmann, U.; Gužvić, M.; Czyż, Z. T.; Feliciello, G.; Polzer, B.; Klein, C. A. High-resolution parallel analysis of genome and transcriptome of single disseminated prostate cancer cells. Single Cell Genomics 2016 Cambridge (UK), September 14-16, 2016
- Knudsen, L.; Lopez-Rodriguez, E.; Berndt, L.; Boden, C.; Ruppert, C.; Hoymann, H. G.; Ochs, M. Alveolar dynamics in progressing bleomycin-induced lung injury: alveolar derecruitment and dynamic alveolar heterogeneity. Meeting of the German Anatomical Society Göttingen (Germany), September 21-24, 2016
- Konzok, S. Behavior of cancer cells in their native microenvironment using human precision-cut lung slices (PCLS) and cell line MDA-MB-231. 15th Fraunhofer Seminar "Models of Lung Disease" Hannover (Germany), January 21-22, 2016
- Konzok, S.; Peter, D.; Braubach, P.; Warnecke, G.; Jonigk, D.; Pfennig, O.; Fieguth, H.-G.; Braun, A.; Sewald, K. Different pathways of inflammasome activation through bacterial and viral PAMPs and cellular DAMPs in human lung tissue ex vivo. 15th Fraunhofer Seminar "Models of Lung Disease" Hannover (Germany), January 21-22, 2016
- Köstler, C.; Stojanovic, N.; Alberter, B.; Hannawald, M.; Schmidt, O.; Brunner, M.; Feliciello, G.; Czyż, Z. T.; Rack, B.; Fehm, T.; Janni, W.; Klein, C. A.; Polzer, B. Molecular analysis of single CTCs of metastatic breast cancer patients. DFG FOR2127 symposium "Selection and adaptation during metastatic cancer progression" Regensburg (Germany), June 1-3, 2016
- Köstler, C.; Stojanovic, N.; Alberter, B.; Schmidt, O.; Brunner, M.; Rack, B.; Fehm, T.; Janni, W.; Klein, C. A.; Polzer, B. Molecular analysis of single CTCs of metastatic breast cancer patients. 10th ISMRC International Symposium on Minimal Residual Cancer Hamburg (Germany), March 19-21, 2016
- Krug, N. Blood eosinophils predict therapeutic effects of a GATA3-specific DNase on both allergic early and late-phase reactions in patients with asthma. 31st Symposium of the Collegium Internationale Allergologicum (CIA) Charleston, South Carolina (USA), April 3-8, 2016
- Kuhn, A.; Klein, C. A.; Spang, R.; Kirsch, S. Modified *Ampli1*TM WGA products enable improved genome coverage for single cells. GCB 2016 – German Conference on Bioinformatics Berlin (Germany), September 12-15, 2016
- Kunz, S.; Rittinghausen, S.; Hoffmann, D.; Schambach, A.; Behr, R.; Müller, T.; Glage, S.; Bleich, A. Proof of pluripotency in experimentally induced teratomas and embryoid bodies by immunohistochemistry. 13th FELASA Congress Brussels (Belgium), June 13-16, 2016
- Kunze, J.; Lahrmann, U.; Klein, C. A.; Kirsch, S. Multisample single-cell analytics – advantages of reproducibility. GCB 2016 – German Conference on Bioinformatics Berlin (Germany), September 12-15, 2016
- Monfort, E.; Escrig, A.; López, A.; Ibañez, M. J.; Bonvicini, G.; Creutzenberg, O.; Ziemann, C. Reduction of crystalline silica toxicity of quartzes. S²R European Forum 2016 Bilbao (Spain), October 26-28, 2016
- Oberholte, H. Cigarette smoke induces inflammation and cytotoxicity in precision-cut lung slices. 15th Fraunhofer Seminar "Models of Lung Disease" Hannover (Germany), January 21-22, 2016
- Oberholte, H.; Braubach, P.; Jonigk, D.; Fieguth, H.-G.; Müller, M.; Braun, A.; Sewald, K.; Wronski, S. HRV1B infection in human precision-cut lung slices is reduced by 3C protease inhibitor rupintrivir. 15th Fraunhofer Seminar "Models of Lung Disease" Hannover (Germany), January 21-22, 2016
- Philipp, F.; Rothe, M.; Hoffmann, D.; Neuhaus, V.; Glage, S.; Rittinghausen, S.; Sewald, K.; Braun, A.; Schambach, A. Human hematopoiesis is influenced by co-injected cell types and Notch-ligand Delta-like1 in a teratoma-based model. 4th Annual Conference of the German Stem Cell Network (GSCN) Hannover (Germany), September 12-14, 2016
- Polzer, B.; Stojanovic, N.; Czyz, Z.; Huber, S.; Scheitler, S.; Alberter, B.; Feliciello, G.; Fahrioglu-Yamaci, R.; Schamberger, T.; Kunze, J.; Lahrmann, U.; Haferkamp, S.; Corbacioglu, S.; Pukrop, T.; Guzvic, M.; Kirsch, S.; Klein, C. A. Infrastructure for biomarker research and a novel diagnostic pathology for systemic cancer. 6th Munich Biomarker Conference Munich (Germany), September 29-30, 2016
- Polzer, B.; Wendler, N.; Fahrioglu-Yamaci, R.; Elsner, F.; Cucuruz, B.; Lindner, M.; Hofmann, H. S.; Passlick, B.; Klein, C. A. Low primary intra-tumoral heterogeneity versus high genomic disparity between primary and distant sites in NSCLC. EACR24: From basic research to precision medicine Manchester (UK), July 9-12, 2016
- Reamon-Büttner, S.; Hiemisch, A.; Rittinghausen, S.; Ziemann, C. Insights into transcriptomic and epigenetic changes in mesotheliomas induced by multi-walled carbon nanotubes (MWCNT) in Wistar rats. 29th Annual Meeting of the German Society for Environmental Mutation Research (GUM) Munich (Germany), October 12-14, 2016
- Reamon-Büttner, S.; Rittinghausen, S.; Ziemann, C. Epigenetic silencing of H-Ras-like suppressor (*Hras*) in mesotheliomas induced by multiwalled carbon nanotubes (MWCNTs) in rats. 2016 International Conference on Environmental Mutagens (EEMGS) Copenhagen (Denmark), August 14-18, 2016
- Requardt, H.; Hansen, T.; Hampel, S.; Steinberg, P.; Dasenbrock, C. Modifying and in-vitro testing of multi-walled carbon nanotubes for their potential use as drug delivery carriers in cancer therapy. BioBarriers 2016 – 11th Conference and Workshop on Biological Barriers Saarbrücken (Germany), March 7-9, 2016
- Rittinghausen, S.; Tillmann, T.; Halter, R.; Schaudien, D. Immunohistochemical characterization of immune system tumors in rasH2 mice. 14th European Congress of Toxicologic Pathology – ESTP 2016 Barcelona (Spain), September 20-23, 2016
- Schaudien, D.; Schwotzer, D.; Ernst, H.; Rittinghausen, S.; Creutzenberg, O. Immunohistological investigation of genotoxicity, cell proliferation and apoptosis induced by inhalation of nanoscaled cerium oxide or barium sulfate. 14th European Congress of Toxicologic Pathology – ESTP 2016 Barcelona (Spain), September 20-23, 2016
- Scheitler, S.; Weidele, K.; Alberter, B.; Werno, C.; Klein, C. A.; Polzer, B. A digital sorting-based detection and isolation assay for single disseminated cancer cells from lymph nodes of melanoma patients. American Association for Cancer Research (AACR) Annual Meeting 2016 New Orleans, Louisiana (USA), April 16-20, 2016
- Schwonbeck, S.; Könnecker, G. PBT substances in veterinary medicinal products – legal basis and recent developments. SETAC Europe 26th Annual Meeting Nantes (France), May 22-26, 2016
- Steffen, L.; Lopez-Rodriguez, E.; Hoymann, H.-G.; Ochs, M.; Ruppert, C.; Knudsen, L. Surfactant replacement therapy (SRT) in the bleomycin model of lung injury and fibrosis. 5th DZL Annual Meeting Hannover (Germany), February 1-2, 2016
- Stojanović, N.; Weidele, K.; Scheitler, S.; Alberter, B.; Raab, M.; Markiewicz, A.; Haferkamp, S.; Renner, P.; Klein, C. A.; Polzer, B. Surface marker-independent enrichment of circulating or disseminated cancer cells from blood or lymph nodes using a micro-fluidic device. EACR24: From basic research to precision medicine Manchester (UK), July 9-12, 2016
- Tentschert, J.; Jungnickel, H.; Laux, P.; Brunner, J.; Reichardt, P.; Estrela-Lopis, I.; Merkers, C.; Ernst, H.; Keller, J.; Ma-Hock, L.; Landsiedel, R.; Gebel, T.; Luch, A. Pulmonary location and extra-pulmonary translocation of CeO₂ nanoparticles following subacute and chronic low-dose inhalation. IPTC 2016 – 11th International Particle Toxicology Conference Singapore, September 26-30, 2016
- Tluczkiewicz, I.; Batke, M.; Kühne, R.; Ebert, R.-U.; Schüürmann, G.; Mangelsdorf, I.; Escher, S. E. TTC: A new concept for inhalation exposure. 15th Fraunhofer Seminar "Models of Lung Disease" Hannover (Germany), January 21-22, 2016

Walter, D.; Fischer, M.; Koch, W.; Dasenbrock, C.
Testing of surface-active compounds in the isolated perfused rat lung.
15th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 21-22, 2016

Weidele, K.; Treitschke, S.; Werno, C.; Botteron, C.; Scheitler, S.; Haferkamp, S.;
Polzer, B.; Werner-Klein, M.; Klein, C. A.
Development of preclinical in-vitro models from rare patient-derived disseminated
tumor cells.
10th ISMRC International Symposium on Minimal Residual Cancer
Hamburg (Germany), March 19-21, 2016

Werno, C.
The potential of single-cell analysis for treatment of metastatic lung cancer.
15th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 21-22, 2016

Werno, C.; Weidele, K.; Treitschke, S.; Botteron, C.; Scheitler, S.; Haferkamp, S.;
Polzer, B.; Werner-Klein, M.; Klein, C. A.
Preclinical in-vitro/in-vivo models from disseminated tumor cells.
6th Munich Biomarker Conference
Munich (Germany), September 29-30, 2016

Wichmann, J.; Jiménez-Delgado, S.; Curths, C.; Schmitt, A.; Dunker, S.; Jonigk, D.;
Braubach, P.; Kaup, F.-J.; Braun, A.; Dahlmann, F.; Eggel, A.; Sewald, K.; Knauf, S.
A novel disruptive IgE inhibitor: efficacy assessment in non-human primate and
human precision-cut lung slices.
5th DZL Annual Meeting
Hannover (Germany), February 1-2, 2016

Wirtz, V.; Jäger, B.; Engelhard, P.; Prasse, A.
A new humanized mice model for idiopathic pulmonary fibrosis (IPF).
15th Fraunhofer Seminar "Models of Lung Disease"
Hannover (Germany), January 21-22, 2016

Active participation in committees

Dr. Luma Baydoun

GMP discussion group "GMP-Gesprächskreis" of the Lower Saxony business
inspectorate

Dr. Annette Bitsch

German Federal Institute for Risk Assessment (BfR) Committee for Food
Additives, Flavorings and Processing Aids

Working committee on probabilistic exposure and risk assessment
"Probabilistische Expositions- und Risikoabschätzung"

Expert panel 110 on cooling lubricants "Kühlschmierstoffe" of the Association
of German Engineers (VDI) Technical Division 1 "Production Technology and
Manufacturing Methods"

Reviewer for international journals published by Elsevier (incl. "Regulatory
Toxicology and Pharmacology")

Dr. Katharina Blümlein

Working group on analyses in biological materials "Analysen in biologischem
Material" of the German Research Foundation (DFG)

Prof. Dr. Armin Braun

Reviewer for international journals in respiratory medicine and immunology
(incl. "Journal of Allergy and Clinical Immunology")

External assessor for international foundations (incl. the Austrian Science
Fund (FWF))

External expert for the German Research Foundation (DFG)

MD/Ph.D. commission "Molecular Medicine" of the Hannover Medical School
Scientific advisory committee of the German Society for Allergology and Clinical
Immunology (DGAKI)

Member of the German Center for Lung Research (DZL)

Dr. Jochen Buschmann

Working committee on reproductive toxicity "AK Reproduktionstoxizität" of the
toxicology advisory board of the German Committee on Hazardous Substances
(AGS)

Dr. Otto Creutzenberg

Reviewer for international journals in particle and fiber toxicology ("Particle and
Fibre Toxicology", "Inhalation Toxicology")

Prof. Dr. Clemens Dasenbrock

Scientific Council on Electromagnetic Fields of the Swedish Radiation Safety
Authority (SSM)

Scientific Expert Group (SEG) of the International Commission on Non-Ionizing
Radiation Protection (ICNIRP)

Working group on the research program on electricity grid expansion "Forschungs-
programm Stromnetzausbau" of the Committee on Non-Ionizing Radiation of
the German Commission on Radiological Protection

Editorial board of the journal "Experimental and Toxicologic Pathology"

Uta Dörfel

Working group on GLP analytics "GLP-Analytik" of the German Society for
Good Research Practice (DGGF)

Dr. Heinrich Ernst

Editorial board of the journal "Experimental and Toxicologic Pathology"

"Guess What" committee of the European Society of Toxicologic Pathology (ESTP)

INHAND (International Harmonization of Nomenclature and Diagnostic Criteria)
organ working groups "Soft Tissue" and "Skeletal System"

Reviewer for the international journal "Toxicologic Pathology"

Dr. Sylvia Escher

Threshold of Toxicological Concern Task Force, ILSI Europe (co-chair)

Dr. Ilona Fleischhauer

Working groups on GLP quality assurance/monitoring "GLP: Qualitätssicherung/
Überwachung" and GCP quality management "GCP-Qualitätsmanagement" of
the German Society for Good Research Practice (DGGF)

Head of the working committee on quality management "Qualitätsmanagement
im VLS" in the Fraunhofer Group for Life Sciences

Dr. Stefan Hahn

Working committee on chemical risk assessment of the German Chemical
Society (GDCh) division of environmental chemistry and ecotoxicology
"Umweltchemie und Ökotoxikologie"

Martina Heina

IT division of the International Association for Pharmaceutical Technology (APV)

Prof. Dr. Dr. Uwe Heinrich

Research Committee of the Health Effects Institute (HEI), Boston, USA

Invited member of the IARC working groups on particles, fibers, diesel engine
exhaust, polycyclic aromatic hydrocarbons, metals, irritant gases, and air pollution
for the compilation of IARC Monographs on the Evaluation of Carcinogenic
Risks to Humans

DFG Senate Commission for the Investigation of Health Hazards of Chemical
Compounds in the Work Area (MAK Commission): working group on the
definition of threshold limit values for dusts; working group on the definition of
occupational exposure limits; working group on the classification of carcinogens;
ad-hoc working group on heavy metals

Committee on Hazardous Substances (AGS) under the German Federal Minister
of Labor and Social Affairs; AGS Subcommittee III (UA III); Subcommittee III:
working groups on metals (chairman) and on fibers/dust

Scientific advisory committee of the German Federal Institute for Drugs and
Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte, BfArM)

Advisory committee of the Institute for Prevention and Occupational Medicine
(IPA) of the German Social Accident Insurance (DGUV)

Committee supporting the public authorities responsible for the approval of
animal experiments (Animal Protection Commission)

Co-editor of the manual on hazard assessment of environmental pollutants
"Gefährdungsabschätzung von Umweltschadstoffen"

Prof. Dr. Jens Hohlfeld

Reviewer for international journals (incl. "American Journal of Respiratory
and Critical Care Medicine", "European Respiratory Journal", and "Journal of
Allergy and Clinical Immunology")

External expert for the German Research Foundation (DFG)

Steering committee of the research network "Biomedical Research in Endstage
And ObsTructive Lung Disease Hannover" (BREATH) within the German Center
for Lung Research (DZL)

Scientific advisory group of the European Medicines Agency (EMA)

Dr. Olaf Holz

Reviewer for international journals (incl. "European Respiratory Journal",
"PLOS ONE", "Respiratory Research", and "BMC Pulmonary Medicine")

European Respiratory Society taskforce "Exhaled biomarkers in lung disease"

IABR (International Association of Breath Research) Standardization Focus Group

Michéla Kaiser

Working group on archiving "Archivierung" of the German Society for Good
Research Practice (DGGF)

Dr. Rupert Kellner

Councilor for electronic communication and member of the Executive Board of the European Society of Toxicologic Pathology (ESTP)

Global Editorial and Steering Committee (GESC) for the initiative "International Harmonization of Nomenclature and Diagnostic Criteria for Lesions in Rats and Mice" (INHAND)

Prof. Dr. Christoph Klein

External assessor for "Lichtenberg Professorships" of the Volkswagen Foundation

External expert for the German Research Foundation (DFG)

Reviewer for international journals in oncology

Prof. Dr. Wolfgang Koch

Reviewer for international journals in aerosol physics and aerosol technology (incl. "Journal of Aerosol Science", "Aerosol Science and Technology" and "Annals of Occupational Hygiene")

Dr. Gustav Könnecker

Working group on European chemicals policy "Europäische Chemikalienpolitik" of the 6th governmental commission "Energie- und Ressourceneffizienz" of the Land Lower Saxony.

Integrated REACH project team, German Federal Office of Bundeswehr Equipment, Information Technology and In-Service Support

Prof. Dr. Norbert Krug

External expert for the German Research Foundation (DFG)

Scientific advisory committee of the German Society for Allergology and Clinical Immunology (DGAKI)

Board member of the interdisciplinary allergy center of the Hannover Medical School

Chair of the Clinical Trial Board of the German Center for Lung Research (DZL)

Steering committee of the research network "Biomedical Research in Endstage And Obstructive Lung Disease Hannover" (BREATH) within the German Center for Lung Research (DZL)

Advisory board of the expertise network "Asthma und COPD"

Dr. Oliver Licht

German Federal Institute for Risk Assessment (BfR) Committee for Contaminants and other Undesirable Substances in the Food Chain; chair of the panel on per- and polyfluorinated alkyl substances "Per- und Polyfluoralkylsubstanzen (PFAS)"

Expert panel "Basic module and perfluorinated tensides" of the German Federal Institute for Risk Assessment's MEAL (= meals for exposure assessment and analysis of foods) study within the Total Diet Study (TDS) in Germany

Working committee on regulatory toxicology "Regulatorische Toxikologie" of the German Society of Toxicology within the German Society of Clinical and Experimental Pharmacology and Toxicology (DGPT)

Public relations delegate of the German Society of Toxicology

Dr. Norbert Lütke

Working group on electronic data processing "EDV" of the German Society for Good Research Practice (DGGF)

Fraunhofer quality management network

Dr. Neophytos Papamichael

Working committee on quality management "Qualitätsmanagement im VLS" in the Fraunhofer Group for Life Sciences

GMP discussion group "GMP-Gesprächskreis" of the Lower Saxony business inspectorate

Dr. Bernhard Polzer

Reviewer for international journals in pathology and oncology ("British Journal of Cancer", "International Journal of Cancer", "Journal of Histochemistry and Cytochemistry", and "Oncotarget")

External assessor for the Wilhelm Sander Foundation for Cancer Research

External assessor for the Medical Research Council (UK)

Priv.-Doz. Dr. Susanne Rittinghausen

Editorial board of the journal "Experimental and Toxicologic Pathology"

Co-optive member of the ESTP board: representative for nomenclature

"Guess What" committee of the European Society of Toxicologic Pathology (ESTP)

Global Editorial and Steering Committee (GESC) for the initiative "International Harmonization of Nomenclature and Diagnostic Criteria for Lesions in Rats and Mice" (INHAND)

INHAND (International Harmonization of Nomenclature and Diagnostic Criteria) organ working groups "Respiratory System", "Endocrine System", "Soft Tissue", and "Special Senses", and working group "Apoptosis"

Associate editor of the international journal "Toxicologic Pathology"

Dirk Schaudien Ph.D.

INHAND (International Harmonization of Nomenclature and Diagnostic Criteria) working group "Non-rodents: minipig"

"Pathology 2.0" committee of the European Society of Toxicologic Pathology (ESTP)

"Webinar" committee of the International Federation of Societies of Toxicologic Pathology (IFSTP)

Dr. Sven Schuchardt

GBM – Society for Biochemistry and Molecular Biology

Leibniz-Institut für Analytische Wissenschaften – ISAS – e.V. (Leibniz Institute for Analytical Sciences)

Reviewer for international journals in biochemistry and analytics (incl. "Journal of Proteome Research", "Proteomics", "Electrophoresis", and "Talanta")

Dr. Katherina Sewald

Reviewer for the international journals "Toxicology Letters", "Toxicology in Vitro", "Nanotoxicology", and "ATOX"

External assessor for international research grants

Steering group of the workshop "Respiratory Toxicity"

Steering group of the workshop "Translational Aspects of in vitro and in vivo Models for Inflammatory Diseases"

Dr. Holger Ziehr

Association of German Engineers (VDI) committee "Technical Good Manufacturing Practice"

GMP discussion group "GMP-Gesprächskreis" of the Lower Saxony business inspectorate

Center for Pharmaceutical Process Engineering (PVZ) at Technische Universität Braunschweig

BioPharma-Translationsinstitut e.V.

Dr. Christina Ziemann

Working group "Genotoxicity" of the DIN Water Practice Standards Committee

Member of the GUM working group on threshold mechanisms of genotoxins

Member of the GUM working group on statistics

Member of the working group on carcinogenesis "Carcinogenese" of the German Society of Toxicology

Teaching activities

Prof. Dr. Armin Braun

Hannover Medical School: lectures in the MD/Ph.D. program "Molecular Medicine"

TRAIN Academy: professional education program "Translational Research & Medicine: From Idea to Product" (lecturer and person in charge of Module 6 "Preclinical development")

Dr. Otto Creutzenberg

University of Leipzig: lecture on inhalation toxicology in the postgraduate course "Toxicology and Environmental Protection"

Lectures on exposure methods/toxicokinetics and on risk assessment and regulation of particulate matter within the DGPT professional education program for toxicology experts ("Fachtoxikologie/in GT")

Dr. Ilona Fleischhauer

German Primate Center, Göttingen: introductory lecture to the GLP guidelines within the "Laboratory Animal Science Course on Primates"

TRAIN Academy: lectures on quality management and Good Laboratory Practice (GLP)

Anke Friede

Hannover Medical School: lecture on quality assurance in clinical trials (audits) within the professional training course "Qualifikation zum Prüfarzt/Prüfärztin bzw. Assistenz in klinischen Studien" (GCP basic class)

Prof. Dr. Jens Hohlfeld

Hannover Medical School: lectures on allergic respiratory diseases

Dr. Stefan Kirsch

University of Regensburg: lectures and hands-on training in molecular oncology in the degree course "Molecular Medicine"; hands-on training in computational biochemistry (database researches) in the degree course "Computational Science"

Prof. Dr. Christoph Klein

University of Regensburg: lectures in pathology and molecular oncology in the degree course "Molecular Medicine"; course and hands-on training in molecular oncology; lectures on pathology in the degree course "Human Medicine"

Prof. Dr. Wolfgang Koch

Clausthal University of Technology: lectures on dispersion of pollutants in the atmosphere

Dr. Oliver Licht

RWTH Aachen: lectures in toxicology and risk assessment

Governmental Institute of Public Health of Lower Saxony (NLGA) in Hannover: lecture on substance assessment and risk assessment within the DGPT course "Regulatory Toxicology"

Dr. Bernhard Polzer

University of Regensburg: lectures in pathology and molecular oncology in the degree course "Molecular Medicine"; course in pathology and hands-on training in molecular oncology; hands-on training in computational biochemistry (database researches) in the degree course "Computational Science"

Prof. Dr. Antje Prasse

Hannover Medical School: lectures on interstitial lung disease

Priv.-Doz. Dr. Susanne Rittinghausen

University of Veterinary Medicine Hannover, Foundation: courses in toxicological pathology

Hannover Medical School: course in laboratory animal pathology

Dr. Anton Roß

Hamburg University of Applied Sciences: lectures in Good Manufacturing Practice (GMP)

Dirk Schaudien Ph.D.

University of Veterinary Medicine Hannover, Foundation: lectures and courses in special and toxicological pathology

Dr. Katherina Sewald

Hannover Medical School: lectures on allergy and asthma and on analgesics in the degree course "Biomedicine"; lectures on hypertension in the degree course "Biochemistry"; laboratory course in biomedicine; laboratory course in biochemistry: immunology

REBIRTH Autumn Academy for Teachers: course and hands-on training

TWINCORE Hannover: LISA – Lower Saxony International Summer Academy

Dr. Natasa Stojanovic

University of Regensburg: course in pathology in the degree course "Molecular Medicine"

Dr. Henning Weigt

TRAIN Academy: lectures on "Principles of quality management – risk management, audits, deviation and change management" and "Preclinical development, phases, costs, and quality assurance"

Dr. Christian Werno

University of Regensburg: lectures on pathology and molecular oncology in the degree course "Molecular Medicine"; hands-on training in molecular oncology

Dr. Holger Ziehr

RWTH Aachen: lectures on "Regulatory Affairs"

Technische Universität Braunschweig: lectures on applied and technical biochemistry

DFG priority program "Mast Cells – Promoters of Health and Modulators of Disease" (SPP 1394)

Characterization of mast cell anatomy and function in primate airways – interaction with the nervous system. DFG Br2126/3-1

Federal Environment Agency

Chronic toxicity/carcinogenicity assessment of selected nanomaterials. R&D project 3712 61 206

Support for the use of computerized calculations such as quantitative structure-activity relationships (QSAR methods) to reduce animal experiments under REACH. R&D project 3714 67 413 0

Animal-free assessment under REACH – further development and application of read-across. R&D project 3715 67 418 0

Human biomonitoring of "novel" substances: substance dossier for Lysmeral – derivation of toxicological assessment values for human biomonitoring. Project number 58 759

Human biomonitoring of "novel" substances: substance dossier for 2,6-di-tert-butyl-4-methylphenol – derivation of toxicological assessment values for human biomonitoring. Project number 59 000

Survey of interactions between different endocrine axes in aquatic test organisms (literature review). Project number 68 006

Federal Institute for Occupational Safety and Health (BAuA)

Evaluation of tier 1 exposure assessment models under REACH. Research project F 2303

Histopathological examination of samples from a long-term inhalation study. Research project F 2325

Method for the identification of granular biopersistent dusts at workplaces. Research project F 2336

Effectiveness of organizational protective measures: efficacy comparison of different methods for cleaning work clothing. Research project F 2346, enhancement (518373)

Comparison of inhalation and instillation as testing methods for characterization of granular biopersistent particles (GBP). Research project F 2364

Mode of toxic action of nanocarbons. Research project F 2376

Comparative research on measurement methods for quantification of the protective effect of personal protective equipment against dermal exposure. Investigation no. 517753

Federal Institute for Risk Assessment (BfR)

Further scientific development of the DevTox project and Website translation into Chinese

Subacute in-vivo toxicity study in male rats with six structurally representative pyrrolizidine alkaloids

Federal Ministry of Education and Research (BMBF) action plan for individualized medicine, funding area "Innovations for individualized medicine"

Collaborative project: TurbiCAR

UniCAR-based treatment of CD19-positive lymphoblastic leukemia – subproject "Production of the anti-CD19 target module"

Federal Ministry of Education and Research (BMBF) funding program "Ersatz und Ergänzungsmethoden zum Tierversuch" (alternatives and complements to animal experiments)

ExlTox – Explain Inhalation Toxicity

Development of an integrated testing strategy for the prediction of toxicity after repeated-dose inhalation exposure: a proof of concept

Federal Ministry of Education and Research (BMBF) funding program NanoCare: "Auswirkungen synthetischer Nanomaterialien auf den Menschen" (impact of synthetic nanomaterials on human health)

Project: InhalT90

90-day inhalation testing with CeO₂ in the rat and subsequent analysis of gene expression profiles for the early detection of toxic/carcinogenic effects

Project: NanoCOLT

Long-term effect of modified carbon black nanoparticles on healthy and damaged lungs

Project: CaNTser

Investigation of the toxic potency of carbon nanotubes following long time inhalation

German Center for Lung Research

Allergy and Asthma

Chronic Obstructive Pulmonary Disease (COPD)

Diffuse Parenchymal Lung Diseases (DPLD)

Publicly funded research projects

National**DFG – German Research Foundation**

Experimental exposure to air pollutants and sympathetic nerve activity in human subjects

Surfactant inactivation, alveolar collapsibility and their role in the progression to pulmonary fibrosis in animal models of lung injury and fibrosis

From Regenerative Biology to Reconstructive Therapy (REBIRTH 2). Excellence cluster

Clinical Research Unit 311, (Pre-)terminal heart and lung failure: mechanical relief and repair

Identification of tumor-specific peptides for adjuvant immunotherapy of melanoma patients without distant metastasis

German Society for Plant and Reactor Safety (GRS)

Study on respirable, aerosol-borne radioactivity release resulting from an explosive event during transportation of nuclear fuel – detection and quantification of the released respirable aerosols

Investigation and assessment of barrier failure and release processes resulting from an event with projectile-forming charges – determination of respirable particle release

Statutory Accident Insurance (DGUV)

Evaluation of usability of the physical characteristics of endogenously generated exhaled aerosols in the diagnosis of occupational lung diseases

Summary and evaluation of toxicological and epidemiological studies and derivation of a point of departure and an exposure-risk relationship (ERR)/occupational exposure limit for phenylhydrazine (CAS 100-63-0) for several relevant health endpoints, with a focus on cancer (2015/ERB 4-2015)

Summary and evaluation of toxicological and epidemiological studies and derivation of a point of departure and an exposure-risk relationship (ERR)/occupational exposure limit for chromium (II) and (III) compounds for several relevant health endpoints, with a focus on cancer (2016/ERB 7-2016)

International**CEFIC-LRI project: B18**

Database on carcinogen dose-response, including information on DNA reactivity, for TTC and beyond

CEFIC-LRI project: ECO18

Identifying limitations of the OECD water-sediment test (OECD 308) and developing suitable alternatives to assess persistence

CEFIC-LRI project: N5-FRAU

Histopathology of rats exposed to barium sulfate nanoparticles by life-time inhalation exposure – effects and biokinetics

EASA project: (CAQ) Preliminary Cabin Air Quality Measurement Campaign

EFSA project: Applying a tested procedure for the identification of potential emerging chemical risks in the food chain to the substances registered under Reach – REACH 2

EFSA project: Testing a procedure for the identification of emerging chemical risks in the food chain

ESIG (European Solvents Industry Group): Verifying the effectiveness of solvent risk management measures

EU program FP7: Primomed

Use of PRImate MOdels to support translational MEDicine and advance disease-modifying therapies for unmet medical needs

EU project: ERA-Net “TRANSCAN”

Analysis of tumor evolution and identification of relapse-initiating tumor cells in non-small cell lung carcinoma

EU project: Eurostars TARGIT

Development of next-generation treatment for allergies: targeted glycan-allergen immunotherapy

EU project: ICONS – Integrated Cooperation On Nanotube Safety

An integrated testing strategy for mechanistically assessing the respiratory toxicity of functionalized multi-walled carbon nanotubes

EU project: Innovative Medicines Initiative (IMI) – eTOX

Integrating bioinformatics and chemoinformatics approaches for the development of expert systems allowing the in silico prediction of toxicities

EU project: Innovative Medicines Initiative (IMI) – Understanding Severe Asthma

Unbiased biomarkers for the prediction of respiratory disease outcomes (U-BIOPRED)

- WP3 Cross-sectional and longitudinal cohort
- WP4 Bronchoscopy studies
- WP5 Clinical models
- WP6 Pre-clinical laboratory models

EU project: PHOENIX

Synergic combination of high-performance flame retardant nanolayered hybrid particles as real alternative to halogen-based flame retardant additives

EU project: PLATOX

In-vitro and in-vivo investigations to generate validated toxicity data of graphene nanoplatelets vs. a carbon black reference

EU project: PneumoNP

Nanotherapeutics to treat antibiotic-resistant Gram-negative infections of the lung

EU project: SILICOAT

Industrial implementation of processes to render RCS safer in manufacturing processes

EU project: SILIFE

Production of quartz powders with reduced crystalline silica toxicity

EU project: ToxRisk (HORIZON 2020)

An Integrated European ‘Flagship’ Programme Driving Mechanism-based Toxicity Testing and Risk Assessment for the 21st century

Cooperation partners

National

ALS Automated Lab Solutions GmbH, Jena

Augsburg University Hospital

BioMedVet Research GmbH, Walsrode

Boehringer Ingelheim Pharma GmbH & Co. KG

Cardior Pharmaceuticals GmbH, Hannover

Center of Allergy & Environment (ZAUM), Munich

Charité, Berlin

Charité Research Organization, Berlin

Clausthal University of Technology

Cytexa GmbH, Freiburg

ECT Oekotoxikologie GmbH, Flörsheim a. M.

Essen University Hospital

EurA Consult AG, Hamburg Office

EURICE – European Research and Project Office GmbH, Saarbrücken

European Aviation Safety Agency (EASA), Cologne

Federal Environment Agency, Berlin and Dessau

Federal Institute for Occupational Safety and Health (BAuA), Berlin and Dortmund

Federal Institute for Risk Assessment (BfR), Berlin

Federal Office for Radiation Protection (BfS), Salzgitter

FOBIG, Forschungs- u. Beratungsinstitut Gefahrstoffe GmbH, Freiburg

Fraunhofer ICT-IMM, Mainz

Fraunhofer Institute for Applied Solid State Physics IAF, Freiburg

Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB, Stuttgart and Würzburg

Fraunhofer Institute for Molecular Biology and Applied Ecology IME, Schmallenberg

Freie Universität Berlin

Friedrich Schiller University Jena

GATC Biotech, Konstanz

GEMoaB Monoclonals GmbH, Dresden

GeneXplain GmbH, Wolfenbüttel

German Cancer Research Center (DKFZ), Heidelberg

German Center for Infection Research (DZIF)

German Center for Lung Research (DZL)

German Primate Center, Göttingen
 Gesellschaft für Anlagen- und Reaktorsicherheit (GRS), Cologne
 Hannover Clinical Trial Center (HCTC), Hannover
 Hannover Medical School
 Heidelberg University Hospital
 Helmholtz Center for Infection Research, Braunschweig
 Helmholtz Zentrum München – German Research Center for Environmental Health, Munich
 IDT Biologika GmbH, Dessau-Rosslau
 Institute for Occupational Safety and Health of the German Social Accident Insurance (IFA), Sankt Augustin
 IPA – Institute for Prevention and Occupational Medicine of the German Social Accident Insurance at Ruhr-Universität Bochum, Bochum
 Karlsruhe Institute of Technology, Division of Combustion Technology at the Engler-Bunte Institute, Karlsruhe
 Kiel University
 Leibniz Institute DSMZ – German Collection of Microorganisms and Cell Cultures, Braunschweig
 Leibniz Institut für Analytische Wissenschaften (ISAS), Dortmund
 Leibniz Research Center for Working Environment and Human Factors (IfADO), Dortmund
 Leibniz Universität Hannover
 LungenClinic Grosshansdorf GmbH
 PAIA Biotech GmbH, Cologne
 Research Center Borstel
 Robert Bosch GmbH – Packaging Technology, Crailsheim
 RWTH Aachen
 SYNENTEC GmbH, Elmshorn
 Technische Universität Braunschweig
 Technische Universität München (TUM), Munich
 TRAIN – biomedical translation alliance in Lower Saxony, Hannover
 TRON – Translational Oncology at the University Medical Center of the Johannes Gutenberg University Mainz, Mainz
 TWINCORE (center for experimental and clinical research on infections), Hannover
 Ulm University
 Universitätsmedizin Göttingen
 University Hospital Carl Gustav Carus Dresden
 University Hospital of Munich (LMU)
 University Medical Center Hamburg-Eppendorf (UKE)
 University of Düsseldorf
 University of Cologne
 University of Freiburg
 University of Giessen
 University of Leipzig
 University of Lübeck
 University of Marburg
 University of Regensburg

University of Tübingen
 University of Veterinary Medicine Hannover, Foundation
 Vakzine Projekt Management GmbH, Hannover
 Vetter Pharma International GmbH, Ravensburg

International
 Adenium Biotech, Copenhagen (Denmark)
 AIT Austrian Institute of Technology GmbH (Austria)
 Angle plc, Guildford (UK)
 AstraZeneca (Sweden)
 Biomedical Primate Research Center, Rijswijk (The Netherlands)
 CeMM – Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna (Austria)
 CIC biomAGUNE, Centro de Investigación Cooperativa en Biomateriales, San Sebastián (Spain)
 Cosmetics Europe, Brussels (Belgium)
 École européenne de chimie, polymères et matériaux (ECPM), Strasbourg (France)
 Erasmus Medical Center, Rotterdam (The Netherlands)
 European Food Safety Authority (EFSA), Parma (Italy)
 Fraunhofer USA – Center for Molecular Biotechnology, Newark, Delaware (USA)
 Fundación CIDETEC (CID), San Sebastián (Spain)
 GlaxoSmithKline Research and Development Ltd., Brentford (UK)
 HANSABIOMED Ltd., Tallinn (Estonia)
 Harvard T. H. Chan School of Public Health, Boston, Massachusetts (USA)
 International Agency for Research on Cancer (IARC), Lyon (France)
 IBMCC (Instituto de Biología Molecular y Celular del Cáncer), Salamanca (Spain)
 Ingeniatics, Sevilla (Spain)
 Institute of Occupational Medicine (IOM), Edinburgh (UK)
 Instituto de Tecnología Cerámica, Castellón (Spain)
 IT'IS Foundation for Research on Information Technologies in Society, Zurich (Switzerland)
 King Mongkut's University of Technology Thonburi (KMUTT), Bangkok (Thailand)
 Life Sciences Queensland, Brisbane (Australia)
 McMaster University Medical Center, Hamilton, Ontario (Canada)
 Medical University of Graz, Graz (Austria)
 Menarini Biomarkers (Singapore)
 Novartis (Switzerland)
 Paris University 13, Paris (France)
 PathoFinder, Maastricht (The Netherlands)
 RIVM National Institute of Public Health and the Environment, Bilthoven (The Netherlands)
 SetLance, Siena (Italy)
 Silicon Biosystems, Castel Maggiore (Italy)
 Stanford University School of Medicine, Stanford, California (USA)
 Swiss Federal Institute of Aquatic Science and Technology (EAWAG), Dübendorf (Switzerland)
 Umaps Communication, Paris (France)

Unilever (UK)

Universidad Autónoma de Madrid, Madrid (Spain)

Université catholique de Louvain, Louvain (Belgium)

University College Cork, Cork (Ireland)

University of Alberta, Alberta (Canada)

University of Amsterdam, Amsterdam (The Netherlands)

University of Basel, Basel (Switzerland)

University of Bern, Bern (Switzerland)

University of Eastern Finland, Kuopio (Finland)

University of Groningen, Groningen (The Netherlands)

University of Rochester, Rochester, New York (USA)

University of Rotterdam, Rotterdam (The Netherlands)

University of Siena, Siena (Italy)

University of Southampton, Southampton (UK)

University of Utrecht, Utrecht (The Netherlands)

US Environmental Protection Agency (EPA), Chapel Hill, North Carolina (USA)

Weizmann Institute of Science, Rehovot (Israel)

World Health Organization (WHO), Geneva (Switzerland)

Yale University, New Haven, Connecticut (USA)

May 22-26, 2016
SETAC Europe 2016
 26th European Annual Meeting of the Society of Environmental Toxicology and Chemistry
 Nantes (France)

June 6-9, 2016
BIO International Convention 2016
 San Francisco, California (USA)

June 8-10, 2016
PCMG 2016
 Annual conference of the Pharmaceutical Contract Management Group
 Rome (Italy)

June 11-15, 2016
EAACI 2016
 European Academy of Allergy and Clinical Immunology Congress
 Vienna (Austria)

June 25-29, 2016
56th Annual Meeting of The Teratology Society
 San Antonio, Texas (USA)

June 29 - July 1, 2016
43rd Annual Meeting of the Japanese Society of Toxicology
 Tokyo (Japan)

June 10-14, 2016
Workshop "Novel approaches to fight bacteria"
 Bremen (Germany)

August 24-27, 2016
EUSAAT 2016
 20th Annual Congress of the European Society for Alternatives to Animal Testing and 17th Annual Congress of EUSAAT
 Linz (Austria)

September 3-7, 2016
ERS Congress 2016
 25th International Congress of the European Respiratory Society
 London (UK)

September 4-7, 2016
EUROTOX 2016
 52nd Congress of the European Societies of Toxicology
 Sevilla (Spain)

September 4-9, 2016
European Aerosol Conference (EAC) 2016
 Tours (France)

September 11-14, 2016
44th Annual Meeting of the European Teratology Society
 Dublin (Ireland)

September 19-21, 2016
OEESC 2016
 Occupational and Environmental Exposure of the Skin to Chemicals
 Manchester (UK)

September 20-23, 2016
ESTP Annual Congress 2016
 Congress of the European Society of Toxicologic Pathology
 Barcelona (Spain)

October 9-13, 2016
ISES 2016
 Annual congress of the International Society of Exposure Science
 Utrecht (The Netherlands)

October 12-14, 2016
BIO-Japan 2016
 Yokohama (Japan)

October 12-14, 2016
29th Meeting of the German Society for Environmental Mutation Research (GUM)
 Munich (Germany)

October 17-20, 2016
ESTIV 2016
 19th International congress of the European Society of Toxicology In Vitro (ESTIV)
 Juan-les-Pins (France)

Exhibitions, congresses and workshops

Fraunhofer ITEM presents its research and the services it offers at national and international congresses and exhibitions. In addition, the institute organizes a variety of seminars and workshops. In 2016, the institute hosted or played an active role in the following events:

January 21-22, 2016
15th Fraunhofer Seminar "Models of Lung Disease"
 Hannover (Germany)

February 1-2, 2016
5th DZL Annual Meeting
 Hannover (Germany)

February 29 - March 3, 2016
82nd Annual Conference of the German Society of Pharmacology and Toxicology (DGPT)
 Berlin (Germany)

March 4-7, 2016
AAAAI 2016
 Annual Meeting of the American Academy of Allergy, Asthma and Immunology
 Los Angeles, California (USA)

March 13-17, 2016
SOT 2016
 55th Annual Meeting of the Society of Toxicology; including Fraunhofer ITEM Exhibitor-Hosted Session on "Testing approaches towards safe nanoproducts"
 New Orleans, Louisiana (USA)

March 16-19, 2016
World Immune Regulation Meeting X (WIRM)
 Davos Platz (Switzerland)

April 12-14, 2016
in-cosmetics 2016
 Paris (France)

May 13-18, 2016
ATS 2016
 International Conference of the American Thoracic Society
 San Francisco, California (USA)

November 3-4, 2016

Quality management in early-phase clinical pharmacology units

Workshop of the Association for Applied Human Pharmacology (AGAH)
Bonn (Germany)

November 7-9, 2016

BIO-Europe 2016

Cologne (Germany)

November 10, 2016

Fraunhofer workshop on "Cell-based in-vitro methods for investigations on biological effects of inhalable compounds"

Hannover (Germany)

Prizes

In 2016, Fraunhofer ITEM researchers were awarded the following prizes for their work:

Elaine Cabral Serrão

Prize: Poster prize for the best poster in the "Effector Mechanisms" session of the EAACI 2016 Congress

Prize for the presented poster entitled "A novel disruptive IgE inhibitor: efficacy assessment in non-human primate and human precision-cut lung slices".

Awarded on June 14, 2016 at the Annual Congress 2016 of the European Academy of Allergy and Clinical Immunology (EAACI) in Vienna (Austria).

Arne Gaida

Prize: Poster prize at the DZL Annual Meeting 2016

Prize for the presented poster entitled "A dual center study to compare breath volatile organic compounds from smokers and non-smokers with and without COPD".

Awarded in February 2016 at the 5th Annual Meeting of the German Center for Lung Research (DZL) in Hannover (Germany).

Dr. Christina Hesse

Prize: "Best Abstract of Young Investigators" in the "Clinical Assembly" session of the ERS 2016 Congress

Prize for the abstract entitled "Induction of pro-fibrotic biomarkers in precision-cut lung slices (PCLS)".

Awarded in September 2016 at the International Congress 2016 of the European Respiratory Society (ERS) in London (UK).

Sandra Huber

Prize: Poster prize at the congress "Shaping the Future with Molecular Medicine 2016"

Prize for the presented poster entitled "Parallel analysis of circulating tumor cells and cell-free DNA from blood samples".

Awarded in October 2016 at the congress "Shaping the Future with Molecular Medicine 2016" in Regensburg (Germany).

Sebastian Konzok

Prize: Poster prize at the DZL Annual Meeting 2016

Prize for the presented poster entitled "Bacterial and viral PAMPs and cellular DAMPs lead to activation of the inflammasome in human lung tissue ex-vivo".

Awarded in February 2016 at the 5th Annual Meeting of the German Center for Lung Research (DZL) in Hannover (Germany).

EDITORIAL NOTES

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