Fraunhofer

IZI

FRAUNHOFER INSTITUTE FOR CELL THERAPY AND IMMUNOLOGY IZI

ANNUAL REPORT 2018

ANNUAL REPORT
2018

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PREFACE

PREFACE

2018 was a very special year for Fraunhofer IZI for all kinds of reasons. There was the change in the institute's management board, which gave fresh impetus to the scientific orientation of the institute, as well as another positive balance sheet. A number of successful developments were also seen across various projects during the course of the year. By the year's end, the institute was able to report a total of 638 employees across six German sites, who turned over a financial volume of 35.2 million euros, wrote over 300 publications and conference papers, and supervised 53 graduations.

The approaches to cancer treatment are just as varied as the forms and manifestations of cancer themselves. Cancer research, and immuno-oncology in particular, therefore has many sides that cannot be covered by one research institution alone. This is why we made it one of our priorities in 2018 to expand the cooperation with clinical research partners in this field even further. Alongside our close partnerships with University Hospital Leipzig and Hannover Medical School, we were also in talks with University Hospital Dresden and Chemnitz Hospital. Besides this, we are working with other partners to develop a network for cell and gene therapy. The value chain is reflected in this network, from development to manufacture and the subsequent translation into early clinical trials, enabling us to take innovative therapeutic approaches directly to the patient. As well as commencing with initial research projects, the various players also grouped together to organize a specialized conference together with the German Society for Gene Therapy (DG-GT), which will be held in 2019 and will focus on the latest concepts in immuno-oncology. The conference will take place at Fraunhofer IZI on September 16 and 17, 2019, and will bring together around 150 international guests from research, medicine and industry.

In January, the Fraunhofer Cluster of Excellence for Immune-Mediated Diseases (IMD) was set up, which the Fraunhofer-Gesellschaft will use to look at the four "D"s of health research in greater detail (drugs, diagnostics, data and devices). Fraunhofer IZI, Fraunhofer ITEM and Fraunhofer IME are working in close collaboration in a kind of virtual institute to drive forward the translation of innovative ideas and individualized therapies for immune diseases and to bridge the gap between pharmaceutical research and actual patient care.

In October, the Fraunhofer project center "Microelectronic and Optical Systems for Biomedicine" (MEOS) was opened in Erfurt, where Fraunhofer institutes IPMS, IOF and IZI will conduct joint research into new biomedical applications in the future. The focus of this project center is placed primarily on key technologies such as microelectronics, photonics and optics. Fraunhofer IZI will contribute its bioscientific expertise here with a view to help develop optical systems for high-resolution microscopy, medical imaging procedures and biosensor technologies.

Numerous new projects were able to be secured and started in the reporting year, while many others were successfully concluded or extended. An especially moving moment for

the members of staff in the Main Department of GMP Cell and Gene Therapy came when approval was granted by the European Commission for the Novartis drug Kymriah® in August 2018. Fraunhofer IZI has been working with the Swiss pharma company since 2015 and is manufacturing the investigational drug for its clinical trials in Europe. The cell / gene therapy for treating various forms of leukemia has now been available to patients since August; a goal that everyone involved had set their sights on.

Based on genetically modified immune cells (CAR-T cells), the drug will be manufactured in the institute's clean rooms on an interim basis until 2021. At the same time, the institute will continue to manufacture investigational drugs for new clinical trials.

Various units at Fraunhofer IZI are otherwise working on developing different genetically modified immune cells. Based on this work, the institute, together with Hannover Medical School, came to secure a Marie Skłodowska-Curie Innovative Training Network – an EU promotional program for young researchers – which will focus on CAR-NK cells.

Another highlight came in setting up a research facility to inactivate pathogens using low-energy electron beams. The prototype marks the successful conclusion of a project funded by the Bill & Melinda Gates Foundation which aimed to improve the manufacture of vaccines. By using low-energy electron irradiation, safer and more effective inactivated vaccines can be manufactured much more quickly. The procedure can now be tested on an industrial scale in the pilot facility and adapted to the different requirements of the major vaccine manufacturers. The project was carried out together with Fraunhofer institutes FEP, IGB and IPA.

In March 2018, the GLP test facility, which has been in operation at Fraunhofer IZI since 2009, was recertified by the Saxon State Ministry of the Environment and Agriculture. As part of the certification process, a division of the Molecular Drug Biochemistry and Therapy Development off-site department (MWT) in Halle (Saale) was also issued with a statement of GLP compliance as an independent test site. Another important milestone was reached in July: For the first time ever, the institute was authorized to manufacture a therapeutic antibody as an investigational medicinal product in accordance with Section 13 of the German Medicinal Products Act (AMG).

The "Molecular Drug Biochemistry and Therapy Development" off-site department was set up in October 2013 to explore and develop new molecular strategies for treating neurodegenerative and inflammatory diseases. Over the course of its five-year start-up phase, the group became a fully-fledged part of the research market and positioned itself well for the future. Following its evaluation in April 2018, and after a unanimous vote by the evaluation committee, the off-site department in Halle (Saale) was included in the regular federal and state financing received by the Fraunhofer-Gesellschaft, safeguarding its future from January 1, 2019. Moreover, the "protein misfolding diseases" junior research group was founded, strengthening the off-site department's portfolio with expertise in the expression, purification and characterization of amyloid proteins.

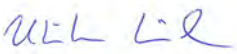
To round off, I would like to offer my personal thanks, once again, to my predecessor and institute founder Professor Frank Emmrich. He has always been on hand to provide me with assistant and support the past couple of years and has done a fantastic job of acquainting me with Fraunhofer and

the way it works. Frank Emmrich had successfully managed the institute since 2005. Infrastructure, staff numbers and research volumes grew and grew under his lead. We wanted to highlight this achievement with the Fraunhofer Life Science Symposium held in September 2018, which was dedicated entirely to his fields of research and once again brought together countless associates and companions. I look forward to standing on my own two feet from 2019 and ensuring the institute continues to go from strength to strength.

Things have certainly gotten off to a good start, a lot of which is thanks to all the staff here at the institute, who have welcomed me, supported me, and helped ensure a smooth transition by continuing seamlessly in their work.

I would like to thank everyone reading this report for their interest and I hope to be able to give you some engaging insights into the work of our institute over the following pages.

Best wishes



Prof. Dr. Dr. Ulrike Köhl

STRUCTURES AND FIGURES 2018

PORTRAIT OF THE INSTITUTE

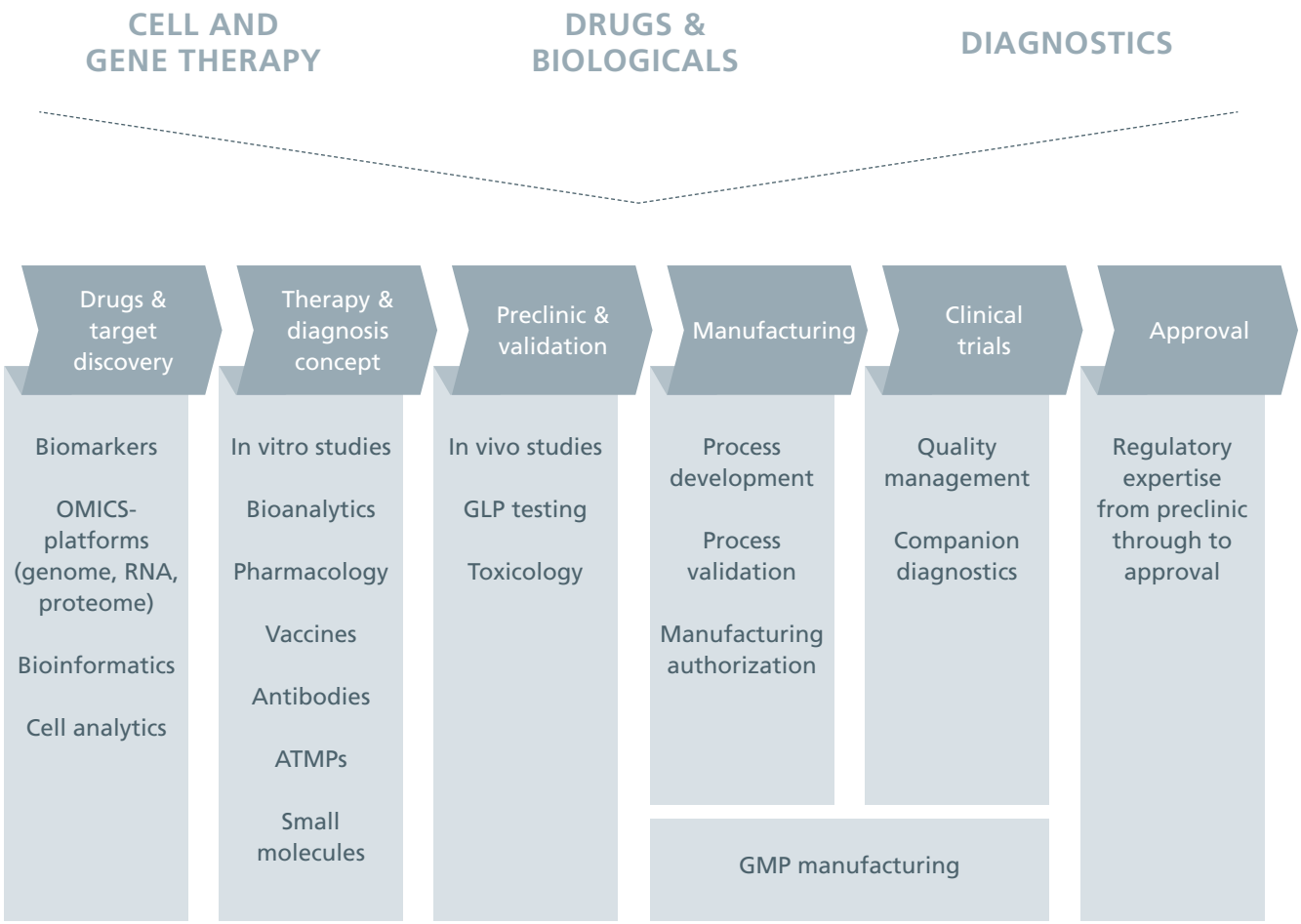
In light of an aging society and an increasing number of chronic diseases, modern medicine is facing exceptional challenges. The Fraunhofer Institute for Cell Therapy and Immunology IZI is working on meeting the demands of health and quality of life through new developments in the fields of diagnostics and therapy. Our body's immune detection and defense system are of particular interest here, as well as cell-biological assay and treatment methods.

The Fraunhofer Institute for Cell Therapy and Immunology IZI investigates and develops solutions to specific problems at the interfaces of medicine, life sciences and engineering. One of the institute's main tasks is to conduct contract research for companies, hospitals, diagnostic laboratories and research institutes operating in the field of biotechnology, pharmaceuticals and medical engineering.

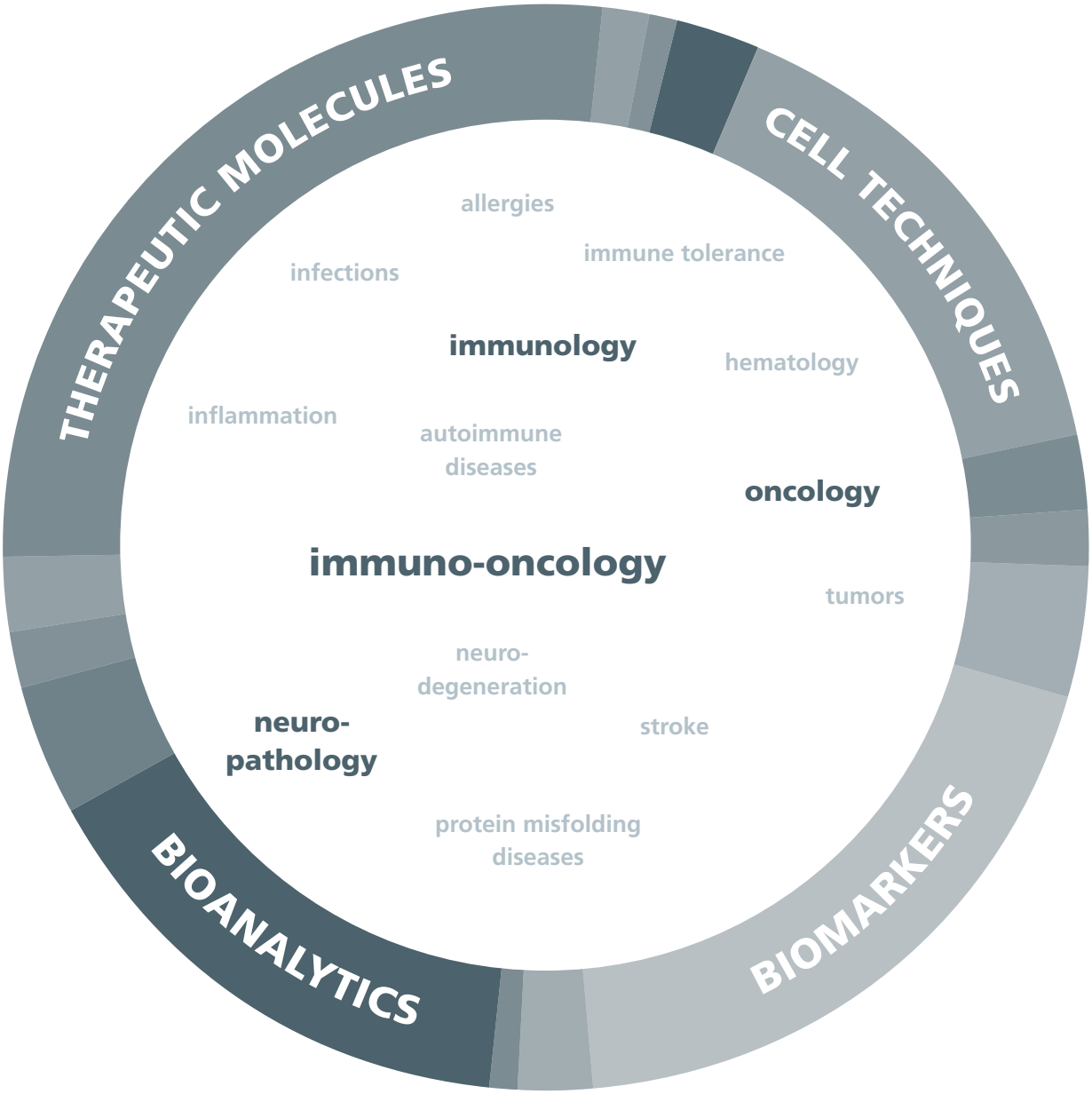
The Fraunhofer IZI develops, optimizes and validates methods, materials and products for the business units Cell and Gene Therapy, Drugs and Diagnostics. Its areas of competence lie in cell biology, immunology, drug biochemistry, bioanalytics and bioproduction as well as process development and automation. In these areas, research specifically focusses on the indications oncology, immunological diseases as well as infectious diseases and neurodegenerative diseases.

The institute works in close cooperation with hospital institutions and performs quality tests besides carrying out the GMP-compliant manufacture of clinical test samples. Furthermore, it helps partners obtain manufacturing licenses and permits.

BUSINESS UNITS



COMPETENCIES AND INDICATIONS



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ORGANIZATION LEIPZIG, GERMANY *

Directors
Prof. Dr. Dr. Ulrike Köhl (executive) | Prof. Dr. Hans-Ulrich Demuth

Administration
Anja Bochmann-Seidel | Annette Schäfer (deputy)

Officers

Executive departments

Business Development and Patent Management
Dr. Thomas Tradler

Press and Public Affairs
Jens Augustin

Occupational Safety
Dr. Peter Ruschpler

IT Management
Alexander Dossin

Central facilities

Center for Experimental Medicine
Dr. Thomas Grunwald

Imaging
Prof. Dr. Ulf-Dietrich Braumann

GLP Test Facility
Dr. Jörg Lehmann

Main Department of GMP Cell and Gene Therapy
Dr. Gerno Schmiedeknecht
Kati Kebbel

Department of Therapy Validation
Dr. Jörg Lehmann

Preclinical Models
Dr. Ulla Slanina

Protein Biomarker
Prof. Dr. Stefan Kalkhof

Antibody Production
Dr. Maximilian Hoffmann

Antibody Development
Dr. Elke Ueberham

Department of Immunology
PD Dr. Sebastian Ulbert

Vaccine Technologies
PD Dr. Sebastian Ulbert

Immune Tolerance
PD Dr. Stephan Fricke

Image Analysis of Cell Function
Prof. Dr. Ulf-Dietrich Braumann

Preclinical Validation
Dr. Thomas Grunwald

Ligand Development
Dr. Michael Szardenings

Antimicrobial Agents
Dr. Andreas Schubert

Biological Material Analytics (ATTRACT group of the Fraunhofer IKTS)
Dr. Juliane Spohn

Department of Cell Therapy
Dr. Thomas Grunwald
Dr. Stephan Klöß

Experimental Imaging
Dr. Sebastian Greiser

Clinic-oriented Therapy Assessment
Dr. Antje Dreyer

Vector-based Tumor Immunotherapy
PD Dr. Ulrich Hacker
Prof. Dr. Hildegard Büning

Branch Lab Translational Cell Therapy (Hannover, Germany)
Dr. Stephan Klöß

Department of Diagnostics
Prof. Dr. Friedemann Horn

Inflammation Models and Immunodiagnostics
Dr. Franziska Lange

MicroDiagnostics
Dr. Dirk Kuhlmeier

DNA Nanodevices
Dr. David M. Smith

CardiOmics
Prof. Dr. Dr. Dr. Andreas Oberbach

RNA Biomarker
Dr. Sophie Bartsch

Next-Generation Diagnostics
Dr. Conny Blumert

Bioinformatics
Dr. Kristin Reiche

LEIPZIG HEADQUARTERS

** January 2019*

1 *Leipzig*


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2


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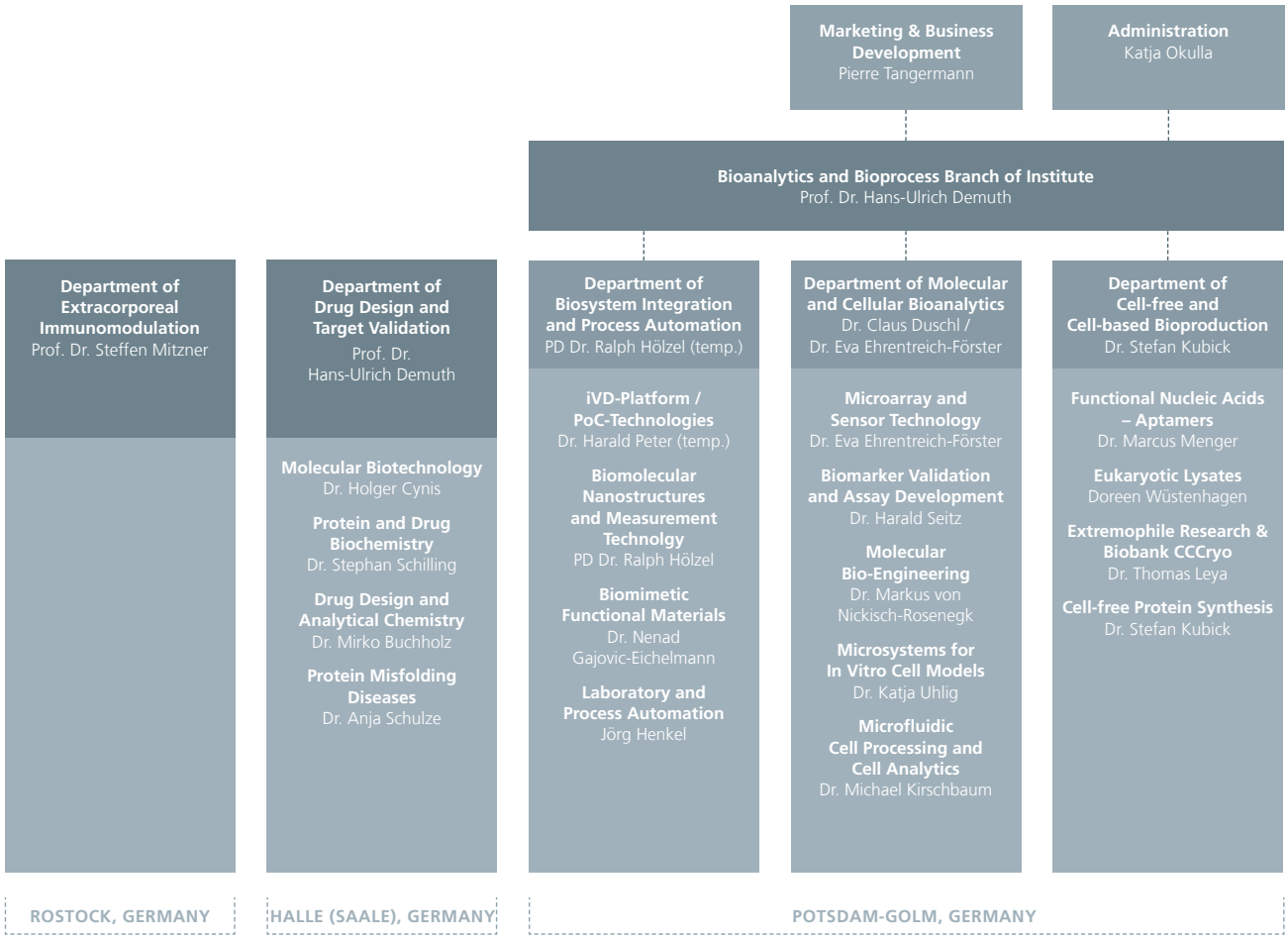
ORGANIZATION BRANCHES *

Rostock / Halle (Saale) / Potsdam-Golm, Germany



1 *Rostock, Germany*
2 *Halle (Saale), Germany*
3 *Potsdam-Golm, Germany*

** January 2019*

KEY INSTITUTE FIGURES 2018 *

PROJECT REVENUE

by funding agency

29.4 %
German national and regional government (TEUR 10 365)

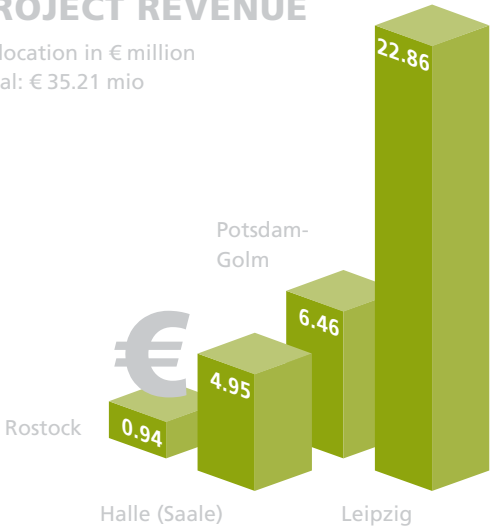
24.3 %
Other (TEUR 8 559)

0.4 %
EU (TEUR 142)

45.9 %
Industry (TEUR 16 143)

PROJECT REVENUE

by location in € million
Total: € 35.21 mio



EMPLOYEES

Workforce composition

53 %
Scientists incl. visiting scientists

7 %
PhD students

16 %
Technical assistants and laboratory technicians

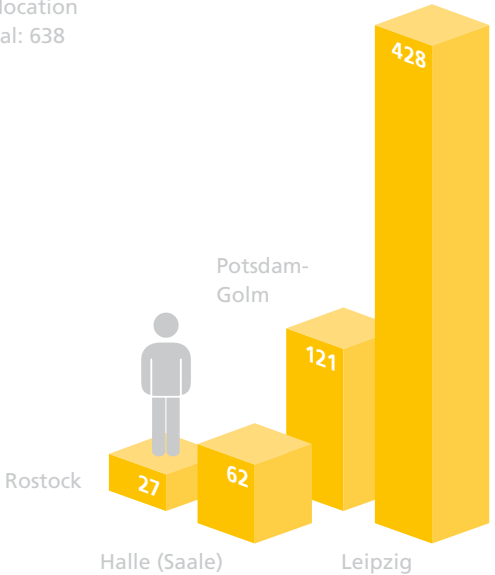
9 %
Student / scientific assistants

10 %
Administration / executive departments / IT and technical infrastructure

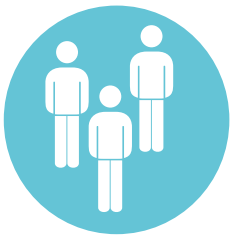
5 %
Interns / degree candidates / Bachelor students / Master students / trainees

EMPLOYEES

by location
Total: 638



SCIENTIFIC PRESENCE AND NETWORK 2018



68
Conventions and conferences

153
Industry partners

155
Research partners

235
Abstracts

89
Publications

13
Book articles

1
Book

11
Doctorates

11
Bachelor theses

28
Master theses

3
Diploma theses

117
Association memberships in various expert associations

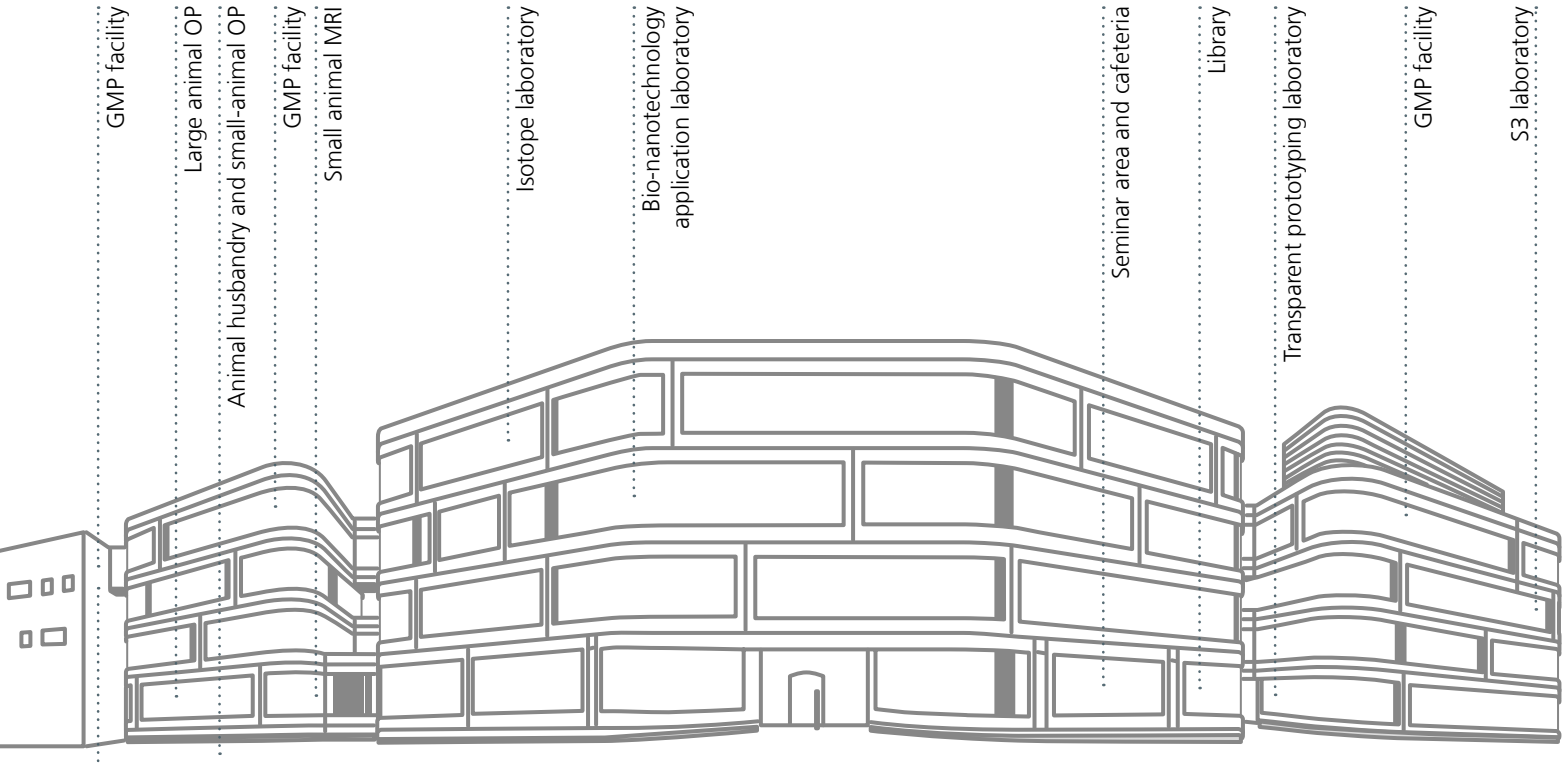
33
Evaluator activities

40
Patent families

174
Patents and patent applications

63
Teaching activities

RESEARCH INFRASTRUCTURE AT THE LEIPZIG SITE



First extension building

- Start-up operations: 2012
- Usable area: 1568 m²
- Lab space: 470 m²
- Offices: 142 m²
- Clean rooms: 410 m²

Rental area at BIO CITY Leipzig

- Start-up operations: 2006
- Clean rooms: 334 m²

Main building

- Start-up operations: 2008
- Usable area: 4131 m²
- Lab space: 1867 m²
- Offices: 1615 m²
- Seminar area: 276 m²

Second extension building

- Start-up operations: 2015
- Usable area: 3050 m²
- Lab space: 1171 m²
- Offices: 881 m²
- Clean rooms: 402 m²

Location Leipzig, Germany

MAIN DEPARTMENT OF GMP CELL AND GENE THERAPY

Quality assurance
1 000 m² clean rooms
ATMPs
Process transfer and development
Manufacturing authorization according to §13 AMG
Investigational Medicinal Drug Dossiers (IMPD)
Good Manufacturing Practice (GMP)

THE DEPARTMENT AT A GLANCE

The main department of GMP Cell and Gene Therapy operates three modern GMP facilities consisting of ten separate clean room suites (altogether 21 clean room grade B manufacturing rooms) which have been specially optimized for manufacturing of cell and gene therapy products, so called Advanced Therapy Medicinal Products – ATMP. The particular specialty of the about 130 highly qualified staff members is the GMP-compliant manufacturing and quality control of investigational medicinal products.

GMP-compliant process and quality control development as well as the creation of Standard Operating Procedures (SOPs) are intensively discussed with the project partner before being implemented. The leading staff in charge has many years of experience in designing GMP-processes in the cell and gene therapy area.

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1

2

PROJECT EXAMPLES

Manufacture of Kymriah®

CAR-T cell therapy is a new type of cancer immunotherapy that uses the patient's own T cells to fight certain types of cancer. In order to do this, the cells are extracted in the clinic by leukapheresis and then genetically reprogrammed in vitro in such a way that they can use a chimeric antigen receptor (CAR) to recognize cancer cells and other cells that have a special antigen on their surface. Following lymphodepleting chemotherapy, the reprogrammed cells are administered to the patient though an infusion. They then proliferate and can trigger the immune response.

In August 2017, the first CAR-T cell therapy became available in the USA in the form of Kymriah® (CTL019 / tisagenlecleucel). Kymriah® was granted FDA approval for children and young adults aged up to 25 years old diagnosed with acute lymphocytic B-cell leukemia (ALL) who are not responding to the usual therapies or have already suffered relapses. In May 2018, approval was also granted for adult patients with diffuse large B-cell lymphoma (DLBCL) who had suffered relapses after two or more lines of systemic therapy or who have not responded to therapy at all. On August 27, 2018, Novartis announced that it had received approval from the European Commission for both these indications.

Fraunhofer IZI has long been an important manufacturing and development site for this innovative CAR-T cell therapy for various clinical trials throughout Europe. Over the next few years, prescription-only, approved T-cell therapies will also be manufactured on an interim basis in the Main Department of GMP Cell and Gene Therapy at Fraunhofer IZI, alongside investigational medicinal products. Following a one-year technology transfer period from Novartis' Morris Plains site in New Jersey, USA, and after obtaining manufacturing authorization in accordance with Section 13 of the German Medicinal Products Act (AMG), the first clinical batch was manufactured at Fraunhofer IZI in Leipzig in August 2016. Sice then, the Main Department of GMP Cell and Gene Therapy has continuously produced CAR-T cell therapies for Novartis.

Until the end of 2018, batches in the high double-digit range were delivered to patients, including many children, all across Europe. The extremely complex process involved in manufacturing a Kymriah®-Batch takes several days and involves not only state-of-the-art instrument engineering, but also manual tasks. Before being released for human use, extensive analytical release tests are first conducted on the finished product (e.g. concerning identity, purity, in vitro potency, microbiological safety) and the batch documentation is reviewed in detail.

Contact

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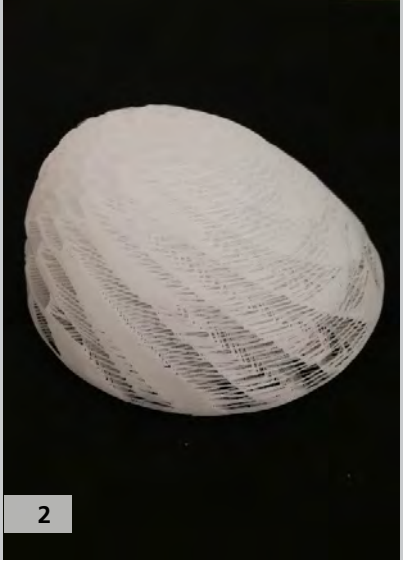
1 *Manufacture of Kymriah® in the clean room.*
2 *Quality of Kymriah® is examined in the quality control laboratory.*

1



2

BioBreast – GMP-compliant production of biodegradable, patient-specific breast implants in the 3D printer for breast reconstruction

According to the German Federal Statistical Office, breast cancer is the most common type of cancer among women. Usually, the only effective treatment methods come in the form of either a lumpectomy (partial removal) or a radical mastectomy. The number of preventive procedures conducted to remove mammary glands due to an increased genetic risk of developing breast cancer, the so-called Angelina effect, is also on the rise. Traditional reconstructive measures are, however, associated with numerous complications and side effects.

The company BellaSeno® GmbH has come up with an innovative technology that takes a patient-specific, bioresorbable polymer implant and fills it by injecting the patient's own fat. The idea behind these implants is to make the surgical procedure as minimally invasive as possible for the patient in future. The porous structure encourages the surrounding tissue to form blood vessels. Once this vascularization process is complete, the patient's own fat, removed by suction, is injected into the breast area. The scaffold degrades over time and is ultimately replaced with natural breast tissue.

The implants are manufactured from a biodegradable polymer using a specially constructed 3D printer. As they are classed as a risk group III medical device, high quality standards are placed on the manufacture of these products. The Main Department of GMP Cell and Gene Therapy has been tasked with the GMP-compliant production of the implants in line with the applicable quality management system. A clean room containing the necessary equipment is available for process transfer. This ensures that production will be carried out under clean-room conditions and that the production environment will be permanently monitored in terms of microbiological and particle aspects to prevent the implants from becoming contaminated with foreign particles as far as possible, thus reducing the risk of rejection reactions. Standardized manufacturing instructions were drawn up in order to document all the process steps relevant to quality. In order to guarantee a consistent level of quality across the printed implants, a quality control concept has been created and implemented, and is set to be developed further in 2019. Additional tasks include qualifying the GMP-compliant manufacturing process as well as any equipment that could impact on quality.

During the course of the project, the implants manufactured in the Main Department of GMP Cell and Gene Therapy will undergo a degradation study, a preclinical long-term study to assess efficacy and safety in a porcine large animal model and a preclinical GLP study to assess safety, all conducted by the Fraunhofer IZI's Department of Therapy Validation (see page 27).

Funded by

Europa fördert Sachsen.
EFRE
Europäischer Fonds für regionale Entwicklung

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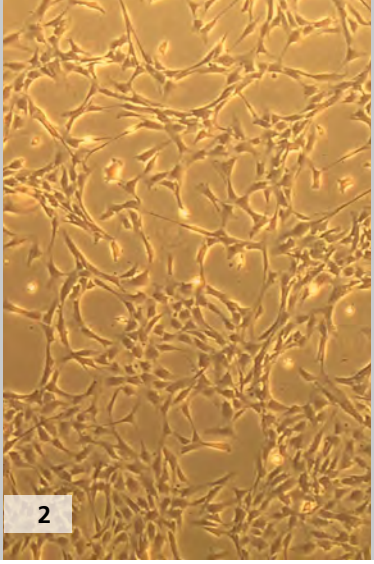
1 *The clean room suite is equipped to manufacture the implants under GMP conditions using 3D printing technology.*

2 *Bioresorbable breast implant made of a biodegradable polymer.*

1



2

autoCard study

Cardiovascular diseases are still the main cause of death in Europe. In Germany, around 60 000 people die from myocardial insufficiency every year. The field of regenerative medicine is, however, showing a great deal of promise here.

The investigational medicinal product "CardAPcells" (cardiac-derived adherent proliferating cells) will be manufactured at Fraunhofer IZI in future in cooperation with Charité - Universitätsmedizin Berlin. The therapeutic agent contains myocardial cells that are isolated from biopsy samples taken from the patient's own heart muscle and expanded over the course of a cultivation process lasting several weeks. Once the required cell concentrations have been reached (usually after four to six weeks), the cells will then be applied as a suspension in their final formulation – intravenously (IV) through a drip on the one hand and intramyocardially, i.e. directly into the heart muscle, using the MYOSTAR™NOGA system on the other. The aim here is to establish the "CardAPcells" investigational product as part of routine patient treatment, giving patients the opportunity to enjoy a better quality of life. There is no risk of rejection as the product uses the patient's own heart cells. The random formation of scar tissue (fibrosis) is probably also reduced.

Test batches were first produced during the project's technology transfer stage. These batches were used to optimize the process and the application of relevant materials and reagents with an eye to the stringent GMP production requirements. The process, which is planned to be conducted in Fraunhofer IZI's clean room, was then validated. Using samples taken from the three validation batches produced, the analytical methods that form part of the safety parameters (checking for mycoplasma, sterility and bacterial endotoxins) were also successfully validated. At the same time, a manufacturing authorization pursuant to Section 13 of the German Medicinal Products Act (AMG) was requested from the responsible state authority, Landesdirektion Sachsen (Saxony Land authorities), which was also on site for the acceptance inspection in February 2018. The inspection went smoothly and Fraunhofer IZI was granted a manufacturing authorization in accordance with Section 13 of the AMG without any further conditions being imposed. The sponsor submitted the study documents to the Paul-Ehrlich-Institut for review in August 2018. Furthermore, authorization to procure tissue samples pursuant to Section 20b of the AMG was also requested from the Berlin State Office for Health and Social Affairs in November 2018.

The first "CardAPcells" tissue procurement cannot be manufactured for patient treatment until this authorization has been granted, a favorable opinion has been issued by the competent ethics committee of the state of Berlin and the autoCard study has received official approval from the Paul-Ehrlich-Institut.

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1 *A member of staff examines the cells through the microscope.*
2 *Adherent CardAPcells in culture.*

Location Leipzig, Germany

DEPARTMENT OF THERAPY VALIDATION

Preclinical studies
Good laboratory practice
Immunotoxicology (study design and implementation)
Protein biomarker (identification and validation)
Antibody development (therapy and diagnostics)
Antibody development and production (therapy)

THE DEPARTMENT AT A GLANCE

The department was founded in January 2016 as a direct replacement of the former Cell Engineering/GLP unit. The main goal of the new department is the concentration of expertise for the preclinical validation of novel therapeutic approaches at IZI, to maximize the efficiency in developing new in vitro or in vivo models and their application in preclinical studies. Since the department manages the GLP test facility of Fraunhofer IZI, all preclinical studies (even those in other IZI departments) can be performed under GLP.

Contact

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The department covers the following topics:

1) Planning and execution of preclinical efficacy and safety studies for new drug candidates (especially ATMPs) and medical devices (ISO 10993) under GLP or GLP-analogous conditions. This includes the development and validation of suitable in vitro and in vivo models.

2) Developing procedures for the diagnostic analysis of secretory and cellular protein biomarkers, including the development and production of specific monoclonal antibodies for their detection and finally the development and validation of the respective diagnostic assays (e.g. ELISA, lateral flow assays, Luminex®, flow cytometry).

3) Identifying and validating new protein biomarkers for diagnosis and therapy of chronic-inflammatory and tumor diseases, as well as for the sector of veterinary medicine / farm animal husbandry.

4) Developing human therapeutic monoclonal antibodies for the treatment of tumor and autoimmune diseases, as well as for passive vaccination against bacterial toxins and pathogenic viruses, and their advancement to drug candidates.

5) GMP-compliant production of clinical test samples, e.g. monoclonal antibodies (manufacturing authorization pursuant to Section 13 of the AMG obtained on July 12, 2018), in a separate clean room facility.

UNITS

Preclinical Models Unit

The Preclinical Models Unit is concerned with the design and implementation of preclinical efficacy and safety studies for new drug candidates under GLP or GLP-analogous conditions. This includes the development, establishment and validation of in vitro and in vivo models for inflammatory and tumorigenic diseases. The main focus of research is on the development and optimization of humanized mouse models for developing and testing patient-specific therapies.

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Click here for further information about the unit.

Protein Biomarker Unit

The Protein Biomarker Unit focuses on the identification and validation of proteins to be used as diagnostic biomarkers or representing therapeutic targets. Moreover, the unit aims at the development of single and multiplex assays for biomarker detection. Multi-omics strategies (especially LC-MS based proteomics) are applied for identification. ELISA, western blot, and peptide or bead arrays (Luminex) are utilized for validation. High-affinity monoclonal antibodies, which are usually developed in the group, are key tools for these immunochemical assays.

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Click here for further information about the unit.

Antibody Production Unit

The Antibody Production Unit operates a state-of-the-art clean room facility for the GMP-compliant manufacturing of monoclonal antibodies based on, for example, CHO cell lines. The modular production facility covers clean room categories D to A and stands out due to its high level of flexibility achieved, amongst others, by using single-use disposables. The range of services includes the planning, development and implementation of manufacturing processes for preclinical and clinical test samples (up to phase II). Test samples can be produced either in bulk or in individual doses.

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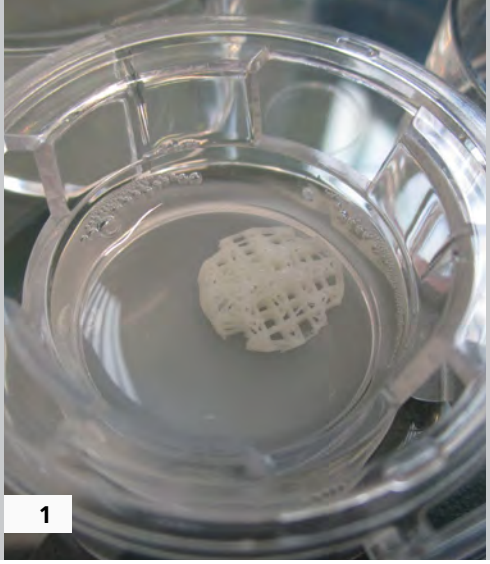
Click here for further information about the unit.



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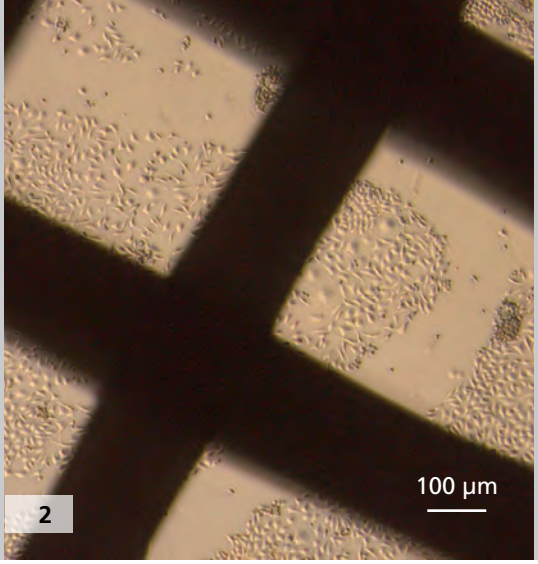

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PROJECT EXAMPLES

BioBreast – preclinical safety trials for a new type of breast implant

Breast cancer is the most common form of cancer among women around the globe, with therapy often involving the surgical removal of breast tissue. Following this kind of mastectomy, there are only a few options for reconstructing the breast. And these are not without their complications. The company BellaSeno GmbH has come up with an innovative solution strategy that presents an alternative to traditional implant products, e.g. silicone, to reconstruct the breast. By implanting a patient-specific scaffold structure made of bioresorbable polycaprolactone that is then filled with the patient's own body fat, the company's approach to reconstruction would entail fewer complications. The final development stage of the implant as well as its manufacture and safety testing for approval as a medical device will be supported as part of an SAB project involving BellaSeno GmbH, GeSIM GmbH and Fraunhofer IZI.

Once BellaSeno GmbH has completed the final development stage, the scaffold structure will be manufactured using a 3D printing method under GMP conditions in the Main Department of GMP Cell and Gene Therapy (see page 23). The implantation strategy and the functionality of the implant will then be evaluated in the large animal model. As the new implant is a risk class III medical device, preclinical and clinical trials have to be carried out in accordance with the German Medical Devices Act in order to ensure biological safety in patients. The preclinical safety trials will be conducted in Fraunhofer IZI's GLP test facility based on DIN EN ISO 10993. The trials characterize and analyze the degradation products used in the resorbable scaffold structure and also test for any potential cytotoxicity in vitro and systemic toxicity in the mouse model. Degradation studies have already been conducted in order to characterize the implant in greater detail; these studies identified the individual degradation products that make up the resorbable implant. Furthermore, the cytotoxic potential of the scaffold structure is currently being investigated in vitro under DIN EN ISO 10993-5. This will be followed by tests on local effects following implantation as well as on systemic toxicity in the mouse.

The aim of the project is to build the foundations for approving an alternative kind of implant to improve the regeneration of breast tissue with few complications. The longer term goal is for the implant to be approved as a medical device and tested as part of a clinical trial.

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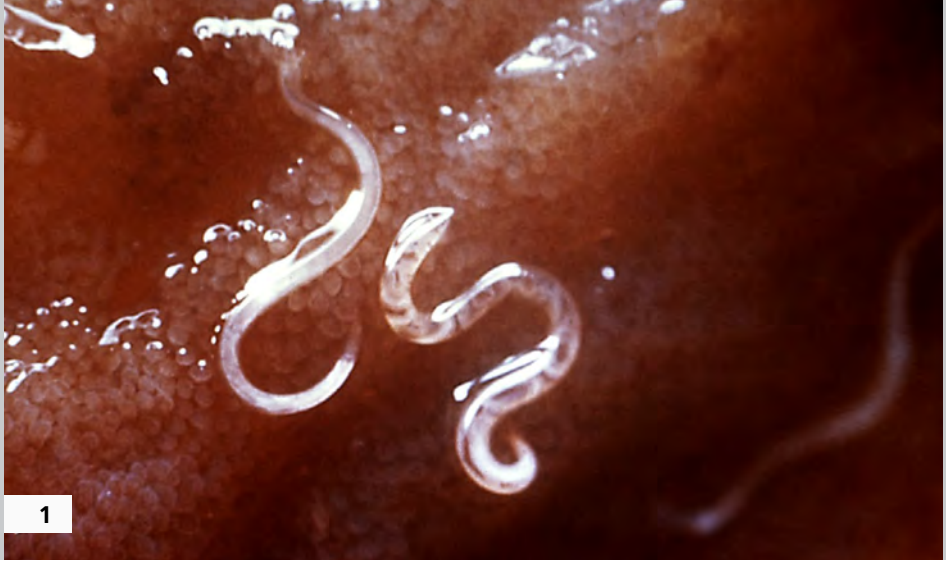
1 *Testing a miniaturized version of the breast implant with an in vitro cytotoxicity assay.*
2 *Microscopic view of the cells under the scaffold structure of the implant.*



1

Improving hookworm monitoring through the development of a rapid diagnostic test ("WormShield")

Worm infections still present a major health-related challenge, especially in tropical and sub-tropical regions. According to statistics published by the Centers for Disease Control and Prevention in 2013, more than 700 million people around the globe are affected by hookworm infections alone, which cause up to 60 000 deaths per year. The infection is transmitted upon coming into contact with water or soil that has been contaminated with feces, which means that it mainly affects rural populations. The infection can be treated effectively with albendazole or mebendazole. The diagnostic methods used at present (Kato Katz, MiniFLOTAC, McMaster) require trained staff and a suitable diagnostic infrastructure, which is why many infections are not diagnosed until very late.

The aim of the international collaboration project "WormShield", which sees the Protein Biomarker Unit collaborate with the company BioScientia (Poland), Cayetano Heredia University (Peru) and Dr. Hugo Mendoza Pediatric Hospital (Dominican Republic), is to improve the diagnosis of hookworm infections in an everyday clinical setting by developing a quick, specific, sensitive, robust and easy-to-use lateral-flow assay. This test is then to be rolled out around the world as a point-of-care diagnostic tool.

The project is being funded by the EU as part of the EU-LAC Health initiative to promote cooperative health research with states from Latin America and the Caribbean.

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1 *The Ancylostoma caninum hookworm attached to the intestinal mucosa. Photo © CDC's Public Health Image Library.*

Location Leipzig, Germany

DEPARTMENT OF IMMUNOLOGY

Antimicrobial peptides
Immunome mapping
Vaccine development
Immunological models
Tolerance induction

THE DEPARTMENT AT A GLANCE

Procedures to stimulate or suppress the immune system are developed in the Department of Immunology. These include vaccines on innovative technology platforms, e.g. novel inactivation methods or plasmid DNA. As such, efficient vaccines can be produced quickly and inexpensively. A further topic is improving the problem-free healing of transplants by the induction of specific tolerance. Furthermore, procedures are being developed to monitor immunoreactivity and to control dysfunctions such as graft-versus-host disease (GvHD). Bacteriostatic peptides and peptide banks for the analysis of immune reactions in food allergies are a further focus. Novel imaging procedures help analyze immunological and cell biological processes.

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UNITS

Vaccine Technologies Unit

The unit develops diagnostic techniques and prevention strategies for infectious diseases in human and veterinary medicine. The main research focus is on viral and bacterial infections affecting livestock and zoonotic diseases. Pathogens up to biosafety level 3 can also be processed. Marker vaccines are developed which enable differentiation between infected and vaccinated animals (DIVA strategy). All state-of-the-art methods in virology, microbiology, molecular biology and immunology are well established in the unit. Viruses currently being focussed on include West Nile Virus, dengue, Zika viruses or influenza. Besides this, strategies are being developed to combat ectoparasites. In addition, large-animal models can be provided through the collaboration with the Faculty of Veterinary Medicine at Leipzig University.

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Ligand Development Unit

Statistical peptide page display is a technology developed at Fraunhofer IZI. It allows the parallel identification of binding peptides of all types. The group applies it for epitope mapping of antibodies directly in sera as well as for finding novel cell specific ligands on the basis of cells, tissues and in vitro organ models.

For working with cells cutting-edge equipment (FACS, imaging) as well as patented methods for the generation of iPS cells or surface modifications for cell cultivation are applied to enable a rapid translation of applied research into commercial usage.

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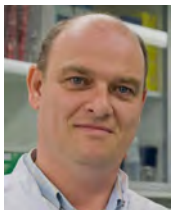
Antimicrobial Agents Unit

The aim of this unit is to develop peptides which have an antimicrobial effect to fight multiresistant germs, such as *Staphylococcus aureus,* vancomycin-resistant enterococci, *Candida albicans,* etc., as well as their evaluation in respective animal models. The main focus here is on applications in the field of dentistry and oral hygiene. A further key focus is placed on identifying and evaluating plant compounds for applications in the fields of immunomodulation, inflammation inhibition, concomitant tumor therapy and antibiosis.

Contact



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Immune Tolerance Unit

The goal of this unit is to develop cell- and antibody-based therapeutic strategies to treat complications following hematopoietic stem cell transplantation. Novel concepts of immunological tolerance which take into account immunological and therapy-associated complications (e.g. GvHD) are being tested in new, in-house developed models.

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Preclinical Validation Unit

This unit develops and examines new vaccines and drugs in preclinical trials. Drugs and vaccine candidates are tested in vitro in cell culture systems and in vivo in preclinical trails involving different animal species, also under GLP conditions This research is focused in part on the development and efficacy testing of innovative vaccines for humans and animals.

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Image Analysis of Cell Function Unit

This unit develops new methods for the non-destructive, microscopy-based quantification of physiological and pathological processes. The aim is to support research into fundamental biological connections and to test new therapy procedures by analyzing cells and tissue without their modification or destruction. As this objective requires interdisciplinary cooperation in the fields of electrical engineering, optics, imaging, software development and biology, the specialist group has close ties to the Chair for Biotronic Systems at Leipzig University of Applied Sciences (HTWK Leipzig).

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Biological Material Analytics Unit

The Fraunhofer IKTS working group is based at Fraunhofer IZI and primarily focuses on developing standardized biocompatibility and immunocompatibility tests for assessing implant materials. This includes developing models based on immune cells and devising ways of standardizing the applied tests. Differentiation processes are combined with immunological tests here. This preclinical in vitro data enables conclusions to be drawn on the functionality of new materials depending on the patient's immune system.

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1

PROJECT EXAMPLES

Electron beams kill off pathogens – new processes for producing inactivated vaccines

Many vaccines are developed as inactivated vaccines, which means that the pathogens they contain have been killed off and can therefore no longer harm the patient's body. In order to produce these vaccines, the pathogens are cultivated in large quantities and then killed off using chemicals. Toxic formaldehyde tends to be used here – in an extremely diluted form to make sure it cannot harm the person being vaccinated. However, such a low concentration also has its disadvantages: The toxin must remain in contact with the pathogen for days or even weeks to take effect, which has a negative impact both on the structure of the pathogen and the reproducibility of the vaccine.

Researchers from Fraunhofer IZI and the IPA, FEP and IGB institutes have developed a procedure that kills of pathogens in fluids without the need for any chemicals whatsoever; these pathogens can then be used in vaccines.

This is achieved using low-energy electron beams. The accelerated electrons break down the DNA and/or RNA of the pathogens, keeping their external structure largely intact. This, in turn, is important as it triggers an effective level of immune protection.

The challenge here lies in the fact that the electrons are only able to reach an extremely low penetration depth in fluids – the fluid level should not exceed 200 micrometers if a uniform dose distribution is to be achieved. The technologies used here did not exist until now; they were developed at Fraunhofer IPA. One of the new methods involves a cylinder being continuously wetted with the pathogen suspension, then irradiated, before the inactivated liquid is transferred into a sterile vessel.

This continuous process is already being used on an industrial laboratory scale. In the fall of 2018, a research and pilot facility was commissioned at Fraunhofer IZI, funded by the Bill & Melinda Gates Foundation. Several liters of pathogen suspension can be inactivated per hour at the facility. Preclinical tests conducted on various viruses and bacteria have shown that the irradiated pathogens lend themselves extremely well to vaccines.

Alongside vaccine development, investigations are under way to determine the extent to which the technology can also be applied to other areas of biomedicine. Using low-energy electron beams, for example, liquid patient samples (e.g. serum) can be freed from infectious agents quickly and easily, e.g. allowing investigations to be carried out in routine laboratories. The technology is also being prepared for use in the field of cell therapy (irradiation of immune cells) at Fraunhofer IZI.

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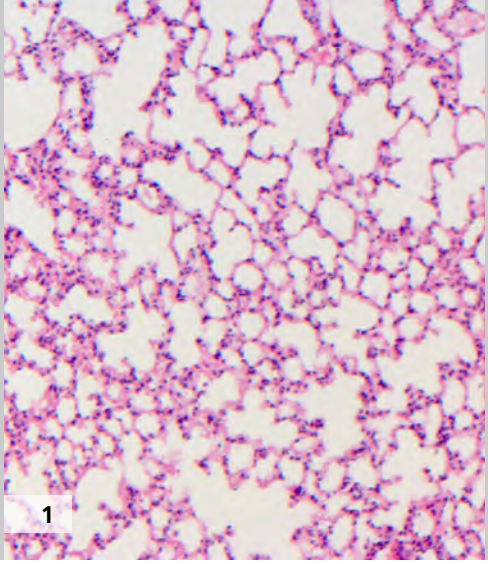
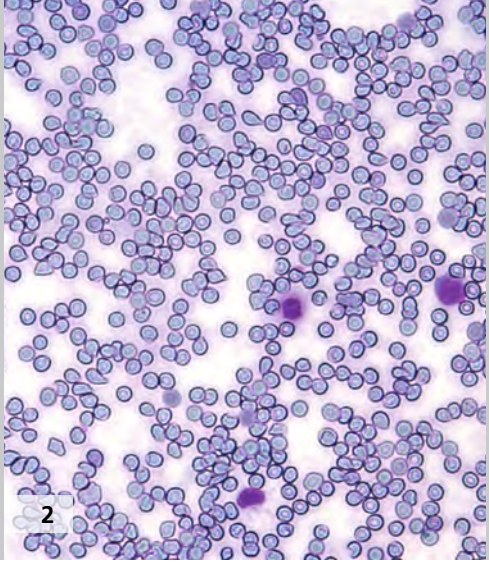
1 *Research and pilot facility for low-energy electron irradiation at Fraunhofer IZI.*





Prevention of adverse immunological complications while retaining the anti-tumor effect following stem cell transplantation using anti-human CD4 antibodies

The main complication following an allogeneic hematopoietic stem cell transplantation is acute graft-versus-host-disease (aGvHD). The conventional treatment methods are frequently associated with low long-term success and toxicities. This necessitates the development of treatment alternatives which are less burdensome.

A new approach involves the use of a specific anti-human CD4 antibody. The antibody specifically reduces adverse immune reactions, thus minimizing the chances of aGvHD emerging following stem cell transplantation. The influence of this anti-human CD4 antibody with regard to the prevention of GvHD and under consideration of the graft-versus-leukemia (GvL) effect in a clinically relevant, humanized leukemia model is currently being investigated.

For this purpose models are being used which are particularly well suited for the transplantation of human hematopoietic stem cells and human leukemia cells. The findings are essential in applying the antibody and other new drugs in a hospital environment. Existing leukemia models are being further developed and the anti-human CD4 antibody and other drugs are being evaluated.

By using humanized models it may be possible to achieve new findings concerning immunological processes in the emergence of GvHD and regarding the GvL effect. The models and findings are not only extremely valuable for hematopoietic stem cell transplantation and leukemia treatment, but also for stem cell transplantation in other indications (e.g. autoimmune diseases).

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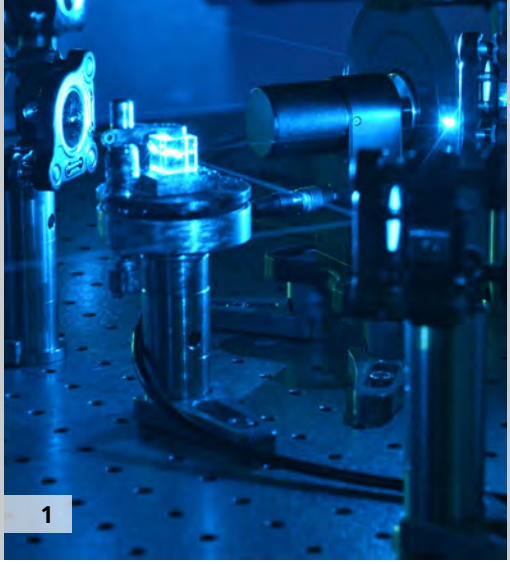
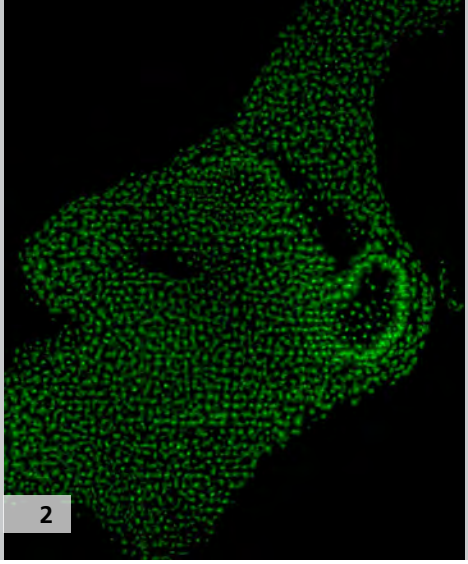
1 *Lung tissue, magnification x10 (HE)*
2 *Blood smear, magnification x100 (Pappenheim)*





Non-destructive cell and tissue monitoring

Over the past few years, the joint specialist group comprising researchers from Fraunhofer IZI and Leipzig University of Applied Sciences (HTWK Leipzig) has developed, among other things, its own modular experimental platform based on single plane illumination microscopy (SPIM). This is a fluorescence microscopy technique that illuminates only the focal plane of the camera with the aid of a thin light sheet (just a few µm). As a result, structures found in front of or behind this plane are not made to fluoresce. This reduces the light-induced stress and bleaching endured by the biological sample on the one hand while increasing the penetration depth the microscope can achieve on the other. Both the penetration depth and image quality can be further enhanced by also clearing the samples.

Depending on the procedure, the microscope's light sheet is alternately introduced into the sample from two sides. The images of one plane produced here are later merged based on a complex algorithm. By gradually moving the sample through the various focal planes, a three-dimensional, high-resolution microscopic image is generated which can then be used for quantitative image analysis and life sciences purposes.

Taking its current state of operation as a starting point, the experimental platform will continue to be developed in the future with downstream image analysis and software development in mind, and with a view to offering both the institute and external customers an extensive range of analytical methods. Students from HTWK Leipzig will actively contribute towards this project through theses and practical research and will also be familiarized with competitive research on an international level.

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1 *Part of the SPIM experimental setup. The beam splitter and chopper wheel can be seen here alongside different mirrors.*
2 *Fused SPIM image of a fetal rat lung.*

1

Mapping of allergen epitopes in sera

Currently immunodiagnostics for diseases are usually based on proteins or extracts, which are directly obtained from the pathogenic organism or produced with biotechnological methods. The disadvantage of this approach is that variants, as they are for example commonly observed for the influenza virus, are difficult to distinguish. We have established protocols to exactly identify the antibody binding sites (epitopes) of patient antibodies, which are also directly applicable to sera. This allows a reliable identification of the pathogen, the causative antigen of allergies or many indications such as (auto)-immune or infectious disease as well as novel approaches for therapy and research.

Food allergies have been one focus of our research over many years. A steady increase of patients could be observed in the recent years. Skin prick tests diagnostics are only of limited use because many plant proteins are very similar in their architecture. Epitope-based diagnostics are most likely the only alternative to elaborate clinical investigations. These usually require venous blood collection, although only the provocation with the food is regarded as proof of an allergy, which has to be carried out under medical supervision in a clinic. An efficient diagnosis, appropriate treatment and adjustment of the food is therefore not available for many patients.

In an initial project we could show as an example for soy allergies that indeed only a few epitopes are sufficient for safely identifying sensitized persons as well as such with clinical symptoms. We are working to use these peptides in a simple test that could detect antibodies in a single drop of blood. Such a test would also be a model for tests on infectious diseases, vaccine efficacy or autoimmune diseases.

A particularly large project is now being funded by the Fraunhofer-Zukunftsstiftung, which is being followed nationally and internationally by allergologists with great interest. In cooperation with several other Fraunhofer Institutes and hospitals, the FoodAllergen project is working on a holistic approach to deal with food allergies. This also includes identifying allergens in foods and new processes of producing food ingredients with reduced allergenic potential. Meanwhile, the epitopes for a wide variety of plant allergens have been identified. An application in tests for patients is in preparation.

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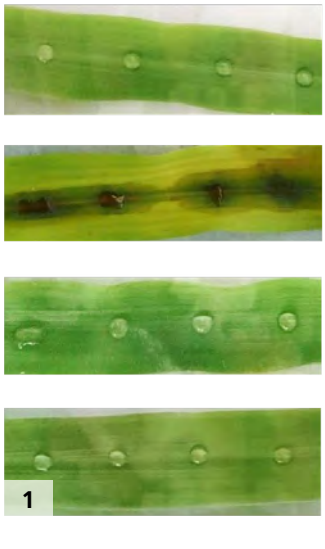
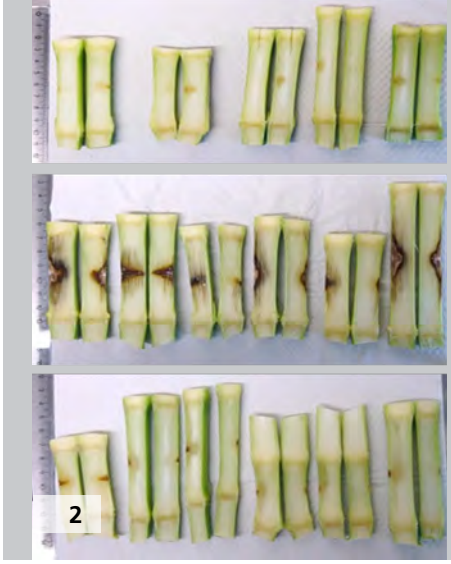
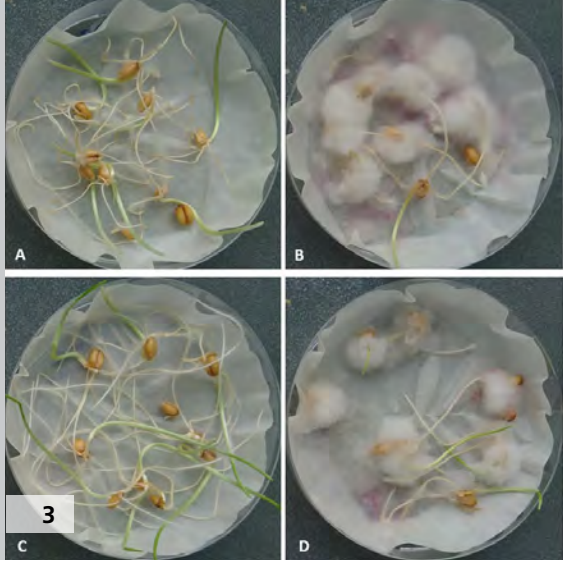
1 *Soybeans. Photo © S.Piyaset – Fotolia*







Identifying and characterizing new active ingredients in African medicinal plants to combat phytopathogenic fungi in agricultural crops

Phytopathogenic fungi and their resistance to conventional fungicides are increasingly becoming a problem and compromising the global supply of agricultural products. This is why researchers around the world are searching for effective alternatives. In Africa, all kinds of plant extracts have long since been used here, especially to combat phytopathogenic fungi and to modulate the rhizosphere.

The objective of this project was to extract fungicidal agents from African medicinal plants and test them in vitro and in planta using a suitable technology platform in order to develop products based on these extracts that could then be marketed in the future. The substantive focus here was placed in particular on plants that could be administered orally in human and veterinary medicine. This already implies low off-target toxicity in humans and animals, which is a key prerequisite if the approval procedure is to be a success.

Extracts were first gained from the barks, leaves and roots of various eastern African plants with the aid of different solvents from the eluotropic series before their toxicity was tested against the conidia and mycelia of relevant phytopathogenic fungi (e.g. *Botrytis cinerea, Fusarium graminearum, Colletotrichum graminicola).* Toxicity testing was conducted both in vitro (microdilution assay) and in planta (leaf infection assay, stem infection assay, fruit infection assay). The toxicity of the extracts was compared to that of conventional fungicides (e.g. tebuconazole). The results showed that plant extracts have an entirely comparable fungicidal effect. The plant extracts actually demonstrated a much better fungicidal effect in the case of fungicide-resistant, harmful fungi species (e.g. *Fusarium graminearum,* PH-1 strain). This is due to the fact that, over the course of evolution, several different fungicidal ingredients acting independently of each another were generally formed in plants as part of a co-evolutionary adaptation process to changing environmental conditions.

The plant extracts studied could be used, among other things, in seed dressing, as a fungicide in conventional crop protection and to treat the surface of citrus fruits. In addition to having a fungicidal effect, several plant extracts also demonstrated root growth induction in the case of wheat germ. Several plant extracts could therefore also be used as plant strengtheners.

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1 *Leaf segment test assay.*
2 *Stalk infection assay.*
3 *Wheat germ infection assay.*

Efficacy of novel helicase-primase based therapy for human Herpes Simplex Virus type (HSV)

Currently, human Herpes Simplex Virus (HSV) infection affects about 82 percent of Germany's population. The pathogen is categorized into two types, which differ in their predilection for the site of infection. HSV type 1 (HSV-1) is associated with a wide range of clinical manifestations including cold sores. In contrast, HSV type 2 (HSV-2) is linked to genital herpes. Both types are able to develop severe disease progression leading to fatal Herpes Simplex Encephalitis (inflammation of the brain). Until now nucleoside analogues, such as Acyclovir and Valacyclovir, are still the treatment of choice for HSV infections. However, due to the existence of nucleoside-resistant viral strains alternative therapies are needed.

Recently, this alternative has been represented by helicase-primase inhibitors (HPIs), which use a novel mechanism of action to inhibit viral replication. In a drug development trial we analyzed the antiviral efficacy of new drug candidates for the treatment of HSV infections in a mouse model. The mice were infected with HSV and treated daily for five days post infection with the compounds of the novel drug class, Valacyclovir or placebo.

Despite the lower dose, we observed a better outcome in clinical parameters in comparison to Valacyclovir control. We could not observe toxic side effects during the monitoring period of 3 weeks post infection. The subsequent analysis showed that treated animals harbor a significantly lower viral load compared with placebo animals.

In this project we showed that treatment with the new development candidates can significantly reduce or prevent clinical symptoms. HPI's are at least one order of magnitude more potent and efficacious compared to Valacyclovir. Thus, candidates of the new drug class are promising inhibitors of HSV infections in vivo and should be translated into clinical trials.

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Location Leipzig and Hannover, Germany

DEPARTMENT OF CELL THERAPY

Experimental imaging
Stroke models
Cell therapeutics
Preclinical study design
Experimental neurosurgery
Histology

THE DEPARTMENT AT A GLANCE

The Department of Cell Therapy prepares new gene and cell therapy procedures for clinical application. This involves the validation of experimental approaches with an eye to safety, feasibility and efficiency. Numerous model systems that facilitate the preclinical testing of novel concepts under the strictest quality criteria have been and continue to be established by the department. These systems lend the obtained results a high level of predictive power with regard to their future clinical application. Cell therapeutic methods are used, for instance, in the case of ischemic diseases such as stroke and myocardial infarction while attention is also given to processes that could prevent cell degeneration and aging. The "sleeping" potential of stem cells is also investigated. Last but not least, the department focuses on cell therapy methods in the field of immuno-oncology, where genetically modified immune cells (cytotoxic T-cells) or natural killer cells (NK cells) are developed to treat tumors.

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UNITS

Experimental Imaging Unit

Experimental imaging stands at the interface between engineering and life sciences. It is dedicated to research activities where the acquisition and processing of images are required before implementation is possible. This draws on different technical devices and software. As the methods used in the applied procedures are constantly being developed, the field of work is always adjusting to reflect the latest developments. The focus here lies on applying state-of-the-art imaging techniques as part of the task assigned to us by our respective project partners.

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Cognitive Genetics Unit

The Cognitive Genetics Unit investigates the foundations and application possibilities for the genetics involved in cognitive processes. The main focus of our work is on the genetics of dyslexia. Our main aim is to develop an early screening test which will effectively facilitate the functional regeneration of dyslexia-related cellular deficits in the future.

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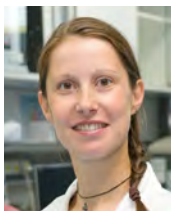
Clinic-oriented Therapy Assessment Unit

The unit tests and develops innovative diagnosis and therapy procedures for ischemic stroke. As the possibility of being able to transfer findings from current laboratory rodent models to human patients is sometimes only very limited, a globally unique large-animal model was established for the translational approach. Tests can be carried out using this model under clinically relevant and patient relevant conditions. Both the gyrencephalic brain structure and the size of the brain much more closely resemble the human situation in the sheep model as opposed to in the small animal.

Contact



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OpTcell Unit

The OpTcell Unit is primarily focused on cancer immuno-therapy. Both patients and science have high hopes for this field in terms of modern cancer therapies. Particularly relevant aspects of cancer immunotherapy are dealt with under three core areas of activity. The aim is to create technological innovations which will potentially increase the efficacy of cancer immunotherapeutics and which may also be used to treat solid tumors.

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Translational Cell Therapy off-site unit (Hannover)

The Translational Cell Therapy off-site unit develops and validates cell-based advanced therapy medicinal products (ATMPs). To do this, it conducts translational research and develops GMP-compliant manufacturing protocols for cell therapeutics at the interface to preclinical development right through to their transfer into clinical trials. Cell and genetic engineering methods and strategies are implemented and optimized here to specifically manufacture killer lymphocytes and their subpopulations. The ability to overcome so-called tumor immune escape mechanisms in cancer cells is key here. This is achieved by using activated and genetically modified effector cells together with checkpoint inhibitors and stimulating immune cells. These cell therapies boost immune surveillance and strengthen the elimination of resistant cancer cells as well as their malignant precursor cells (so-called tumor stem cells). Another focus of development lies in optimizing the transduction capacity of effector cells using chimeric antigen receptors (CARs) in order to increase cytotoxicity to malignant cells. To do this, human effector cells are separated following lymphapheresis by means of GMP-suitable, fully automated, closed-system production, genetically modified as necessary and expanded as part of clinical upscaling. Moreover, the group is developing GMP-compliant manufacturing and expansion protocols in order to proliferate a sufficient number of activated effector cells.

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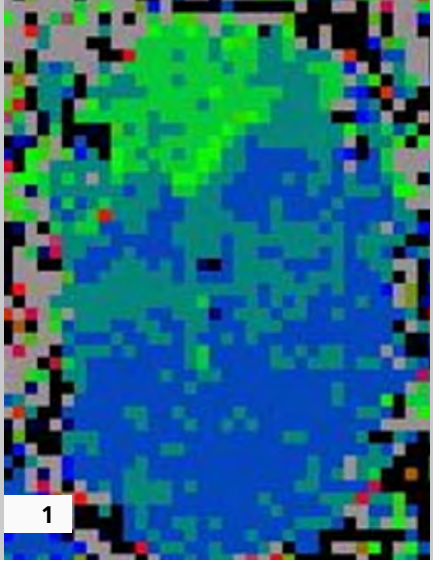

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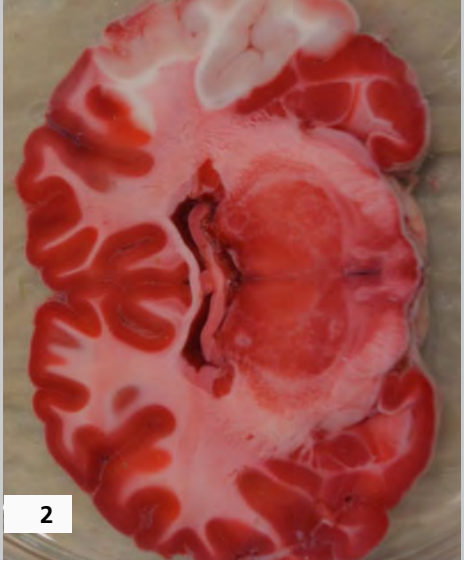

2

PROJECT EXAMPLES

Evaluation of therapeutic drugs in transient stroke model in sheep

The human brain needs a blood supply of 80ml/100g brain tissue and minute. Massive functional and tissue loss occurs by serious restriction of the blood flow (e.g. an occlusion of a cerebral artery) in a circumscribed brain area: A stroke occurs. Brain areas, which are completely interrupted by blood and with this oxygen supply, die very quickly. The affected brain tissue can be rescued from die-off if the oxygen level in the affected area is increased immediately. Hence, an intermediate and sustained accumulation of oxygen recovery is crucial to the patient's recovery. The current available treatments such as the reopening of the blood vessel have a very limited time window of 4.5 hours after onset and a lot of contraindications. Therefore, approximately only 30 percent of the stroke patients are treated.

The company Omniox Inc. and the Fraunhofer Institute for Cell Therapy and Immunology are striving to improve this situation with a new therapy concept. This concept is based on a treatment that increases the oxygen level specifically in low- or non-perfused tissue at an early stage thereby extending the time window for reopening the blood vessel and limiting the affected stroke area. On the basis of highly diagnostic models, the safety as well as the efficacy of the described procedure is verified. In doing so, a specialized imaging procedure for a localization-based description of blood supply and diffusion capacity and therefore oxygen supply is performed in cooperation with the Clinic of Nuclear Medicine at the University of Leipzig. On the basis of these investigations, the treatment can be optimized accordingly and the development of a therapeutic agent can be driven forward.

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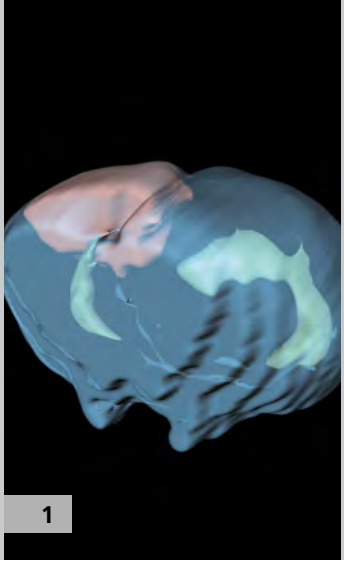
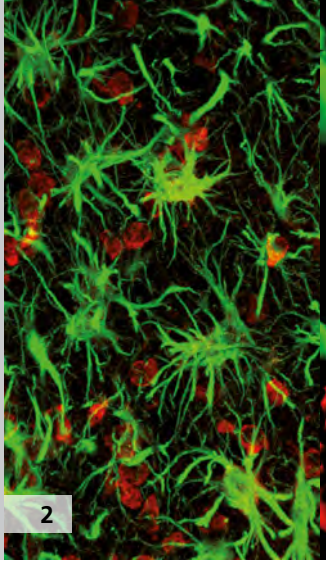
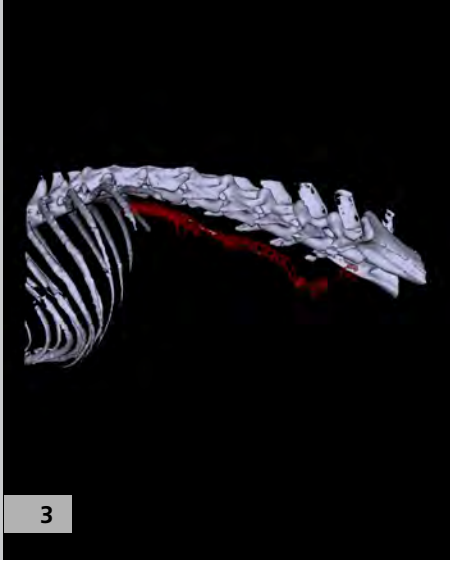
1 *MRI image of acute stroke in the sheep; green areas reduced or not perfused at all.*
2 *Depiction of the corresponding cerebral lamella following TTC staining; red areas vital tissue, white areas dead tissue.*







Modern imaging procedures for diagnostics and preclinical research

The field of life sciences presents us with a number of imaging methods. Procedures applied in this field draw on a broad span of the electromagnetic spectrum, ranging from short-wave roentgen radiation (computer tomography) to light that is visible to humans (microscopy), right over to the radio frequency range (magnetic resonance imaging). Each one of these procedures is able to pinpoint structures or biological processes in the living organism with great precision. Data can be collected here to create a virtual 3D rendering of the investigated structures.

Based on this image, pathological processes such as those which emerge in the case of a stroke and are being investigated by the Clinic-oriented Therapy Assessment Unit at Fraunhofer IZI can be precisely quantified. With the aid of magnetic resonance imaging (MRI), different contrast methods and special segmentation algorithms, the damaged area can be depicted in vivo (image 1). Far-reaching rebuilding processes take place in the affected areas of the brain once brain tissue is damaged, for instance due to hypoxia during a stroke. To be able to depict regeneration on a microscopic level, the respective region is marked immunohistochemically and scanned using a confocal laser scanning microscope (LSM). This makes it possible to specifically describe the number and morphology of cells, their interaction with other cells, and their changes over the course of time (image 2). The processes facilitate the quantification of pathological changes following brain damage and therefore lend themselves well to verifying the efficacy of new therapeutic procedures.

Beyond stroke research, other diseases and their progression can also be monitored through experimental imaging procedures. For instance, in the case of chronic kidney disease, both an increase in kidney volume and also calcifications in the aorta emerge as time goes by. In a study conducted by the Inflammation Models and Immunodiagnostics Unit, both these disease markers were able to be diagnosed (image 3) with the aid of computed tomography (CT). The next step here is to conduct investigations to identify a more effective treatment for chronic kidney disease.

In future, the competencies of the Experimental Imaging Unit are to be pooled further with those of the Image Analysis of Cell Function Unit and merged into the central imaging and image evaluation facility.

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1 *Visualization of a stroke in a 3D model of a rat's brain.*
2 *3D model of astrocytes based on immunohistochemical staining.*
3 *Evidence of calcifications in the aorta of a rat with chronic kidney disease.*

LEGASCREEN – Development of an early screening test for dyslexia

Dyslexia is a severe disorder of reading and writing, affecting about 5 percent of all German schoolchildren. It is one of the most common developmental disorders in childhood and youth. Dyslexia is unrelated to the child's intelligence. It results in tremendous problems in school, education and at work.

One of the main problems hampering successful therapy is late diagnosis: With current methodology, dyslexia can be reliably diagnosed at the earliest at the end of the second grade. By this time, a large part of speech development has already passed, and a lot of precious time for early therapy is inevitably lost.

Benefiting from previous research on the genetics of dyslexia, this project aims to overcome these limitations. The earlier that a risk for dyslexia is diagnosed, the earlier therapy can be initiated to reduce later problems. The project is a joint project between the Fraunhofer-Gesellschaft and the Max Planck Society. It integrates different research areas: Genetics as well as specific measures of brain activation (EEG).

Heritability of dyslexia is estimated at between 50 and 70 percent. Genetic information does not basically change during the life span. Consequently, specific genetic variants can be measured long before reading and writing is taught. The project will leverage known genetic risk variants as well as further optimize those genetic markers.

The other important part of the test is based on electro-encephalography (EEG). Here, brain activation is analysed, even without drawing attention to a stimulus. It is known that children with a risk for dyslexia, even as infants, have specifically altered brain activation patterns in response to specific language stimuli.

Finally, the project includes magnetic resonance imaging (MRI). MRI assessments will not be part of the final test but are very helpful during assay development. Information about brain structure provided by MRI can hint to connections between genetics and activation patterns seen in the EEG measures.

To summarize, the aim of this project is to develop an early screening test for dyslexia. This test should be applicable long before conventional testing is carried out. It is believed that early testing will improve the access to as well as the success of dyslexia therapy.

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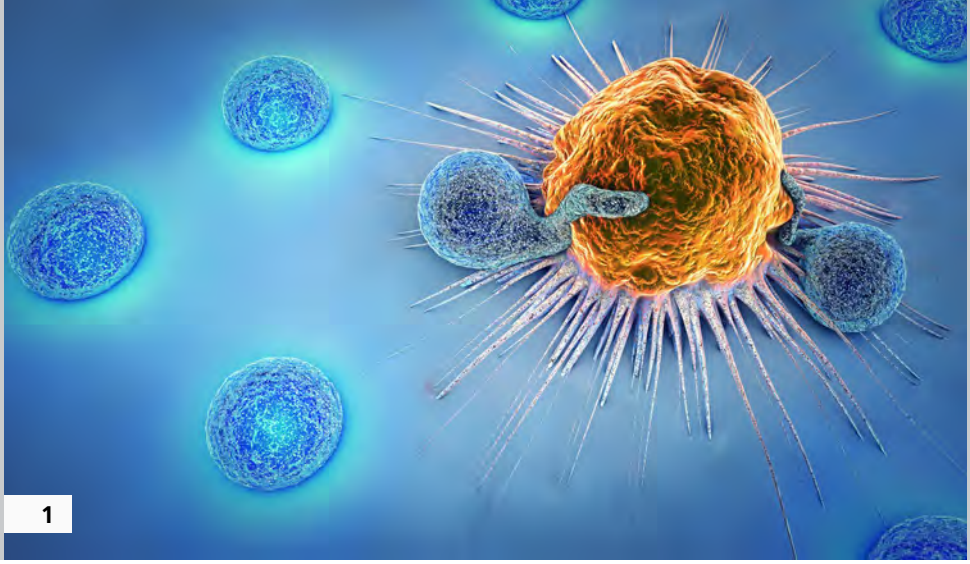
1 *EEG examination.*
2 *MRI examination.*



1

Ex vivo expansion of PBMC-derived human NK cells for use in in vivo studies

One of the main functions of the human immune system is to defend against infections. Another is to eliminate cancer cells.

Immune cells are fundamentally capable of recognizing cancer cells and eliminating them through various mechanisms. One of these mechanisms is antibody-dependent, cell-mediated cytotoxicity (ADCC), whereby antibodies bind to the surface of cancer cells, giving natural killer (NK) cells a signal to kill the respective cells. These immune cells bind to the cancer cells via the antibodies and are stimulated to release cytotoxic proteins.

Despite some cancer cells being able to evade this mechanism due to their immunosuppressive properties, it offers an excellent starting point for developing new forms of cancer therapy based on this immunological principle.

To this end, the company Affimed developed a new antibody platform for killing malignant target cells with extreme precision. This platform enables the immunosuppressive mechanisms employed by tumor cells are overcome and a targeted immune response to be triggered.

As part of the project, leukapheresis was conducted on different, healthy donors at Fraunhofer IZI's off-site unit in Hannover. NK cells were then separated immunomagnetically from the enriched peripheral blood mononuclear cells (PBMCs), expanded for two ex vivo weeks, and then cryopreserved. The cells could then be thawed, expanded / activated anew and investigated as part of preclinical tests as and when required.

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1 *Schematic depiction of a cancer cell identified and attacked by immune cells. Photo © Christoph Burgstedt - stock.adobe.com*

Development of a therapy concept for neurodegenerative diseases based on the extracellular vesicles of mesenchymal stem cells

Exosomes are 30 to 90 nm large compartments (vesicles) that originate from a cell and are released into the extracellular environment. They are able to "communicate" with other cells as they contain different molecules to the original cell. This characteristic has led to these extracellular vesicles gaining significance both diagnostically and therapeutically.

At Fraunhofer IZI, extracellular vesicles are used by mesenchymal stem cells (MSCs) as a vehicle for transferring molecules into the central nervous system (CNS).

MSCs are a heterogeneous cell population that exist in almost all tissue types. They possess excellent self-renewal properties and can be cultivated easily. Thanks to their ability to encourage tissue regeneration and reduce inflammation, MSCs present an attractive resource for cell therapy applications. It has been shown that vesicles derived from MSCs have the capacity to modify the inflammatory responses of microglial cells (Jaimes et al 2017). This is extremely important for neuroinflammatory diseases as microglial cells, the immune cells of the central nervous system, play an important role in the emergence of neurodegenerative diseases.

The aim of this project is to develop a cell-free and vesicle-mediated approach to treating degenerative diseases such as Alzheimer's. The idea here is to equip MSC-based vesicles with anti-inflammatory molecules by means of lentiviral vectors in order to induce the degeneration of Aβ aggregates in the brain without activating microglial cells.

Funding

This project is being co-financed using tax revenues based on the budget adopted by the delegates of Saxony's state parliament.

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DEPARTMENT OF DIAGNOSTICS

Transcriptome analyses
Next-generation-diagnostics
Bioinformatics
Nanotechnology
Lab-on-chip
Biomarker identification
Tumor models

AUGGCUA
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AUGGCUA

THE DEPARTMENT AT A GLANCE

The Department of Diagnostics offers a value chain that comprises the screening and testing of biomarkers, bioinformatic analysis and interpretation of complex transcriptome and genome data ("big data"), development of in vitro diagnostics (IVD) and point-of-care platforms as well as appropriate preclinical animal models.

Within the department, the RIBOLUTION Biomarker Center was established in the course of the Fraunhofer-Zukunftsstiftung- (Future Foundation-) funded consortium RIBOLUTION (RIBOnucleic acid-based diagnostic soLUTIONs) to systematically identify and validate novel diagnostic or prognostic biomarkers. Noncoding RNAs that possess a promising and long underestimated biomarker potential are a particular focus. The RIBOLUTION Biomarker Center provides experienced bioinformatics for analyzing NGS and other complex data sets. Competencies in study and data management serve to design and conduct clinical cohorts as well as to manage clinical and experimental data. For the development of diagnostic assays, a quality management system following DIN EN ISO13485 rules has been implemented.

The development of innovative molecular diagnostic test systems is offered for medical and food applications and comprises PCR- and NGS-based IVDs, lab-on-a-chip-platforms, and strip-based flash tests. The department aims at diagnostic solutions in many clinical fields, including cancer, infectious and inflammatory diseases.

It also offers the development of companion diagnostics and provides many established cell and animal models in various areas like tumor stem cells, rheumatoid arthritis and other chronic-inflammtory diseases as well as many more. Furthermore, xenogene transplantation models serve to close the gap between model and patient.

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UNITS

Inflammation Models and Immunodiagnostics Unit

This unit develops rapid, straightforward, immunological, cell biological and genetic analysis and model systems for the areas of graft rejection, inflammation research and tumor biology, in particular for joint and pulmonary diseases. This involves the use of innovative immunoassays, genetic analyses, complex cell culture models and animal experimental approaches.

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RNA Biomarker Unit

Our focus is on the identification and validation of new diagnostic and prognostic RNA biomarkers for various diseases. We use a wide range of molecular methods (nextgeneration sequencing, microarrays, PCR-based methods) for the GLP-oriented screening and validation process. We also focus on companion diagnostics, which is an important step towards personalized health care. With the development of specific tests (e.g. cancer diagnostics), we are constantly moving towards the optimal goal.

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Next-Generation Diagnostics Unit

This unit develops and establishes analysis strategies for discovering novel biomarkers to diagnose and anticipate diseases. The focus here is placed on the detection and characterization of RNAs, especially of non-protein-coding RNAs (ncRNAs), which possess a great deal of potential in terms of their use as biomarkers. The latest nucleic acid analysis techniques are employed here based on next-generation sequencing and microarrays. These procedures are being optimized to analyze various base materials (cryo tissue, FFPE tissue, urine, blood).

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Tumor Stem Cells Unit

This unit's objective is to develop therapeutic strategies based on cells and agents for the treatment of neoplastic diseases based on the elimination or modification of tumor stem cells in the relevant malignant tumor. This concept is to be used to describe the tumor stem cells of further tumor entities and to facilitate therapeutic innovations in the field of internal oncology.

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DNA Nanodevices Unit

This unit focuses on exploring and developing DNA-based tools for biomedical research. In doing this, DNA molecules and their characteristics are used to arrange and structure biomaterials on the nanometer scale. This type of technology is applied to develop biosensors and nanocircuitry for bio-chips, in addition to being used to develop new procedures to specifically transport molecules in vivo and in vitro. To this end, the unit investigates the biochemical and biophysical characteristics of specific DNA molecules and composite materials in order to deduce concrete applications.

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MicroDiagnostics Unit

This unit develops molecular diagnostic test systems for the food and medicine/clinical practice sectors. A major focus is rapid tools to detect infectious agents or diseases-specific biomarkers including methods for bioanalytical sample preparation. Work is being done with customers to create novel reagent-free cell lysis methods and lab-on-a-chip diagnostics platforms, e.g. to detect sexually transmitted pathogens in a home-testing format. The field of immunomic and oncological exosome analytics form a further focus. The unit has access to hot embossing methods.

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Bioinformatics Unit

The Bioinformatics Unit develops and establishes computer aided ways of identifying and verifying new biomarkers for the personalized diagnosis and prognosis of diseases and for the detection of novel therapeutic targets. The fact that a vast number of RNA molecules are not translated into proteins has only been known for a few years. The latest scientific findings show that these non-coding RNAs (ncRNAs) perform fine regulatory tasks in gene regulation and are therefore suitable as markers for individual disease patterns and progression. The unit develops strategies for efficient processing and (statistical) analyzing molecular biological data gained from extensive clinical cohorts based on next-generation sequencing, microarrays, and DNA, RNA, and epigenetic analytics in order to detect disease-relevant ncRNAs. The gene regulatory mechanisms of ncRNAs are modeled using methods from systems biology and RNA bioinformatics. The objective of the unit is to analyze the potential of these innovative RNA molecules as biomarkers or therapeutic targets and to establish them as appropriate clinical markers or targets.

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CardiOmics Unit

The unit carries out research into infectious diseases relevant to cardiac surgery using state-of-the-art OMICS technology platforms. Infective endocarditis and the development of molecular biological diagnostic procedures are of particular scientific interest here, as is the translation of such procedures into routine clinical practice. Based on improved diagnostics, alternative treatment methods are evaluated and new interventional procedures taken to clinical maturity.

The unit will concentrate on the connection between infectious diseases and molecular regulatory mechanisms associated with haemostasis. In the interdisciplinary field of intervention strategies relating to cardiac surgery, the diagnosis and therapeutic intervention of the coagulation system play a vital role. The unit primarily develops diagnostic procedures to determine the effect of factor X inhibitors and /or coagulation diagnostics during the final stages of plasma coagulation.

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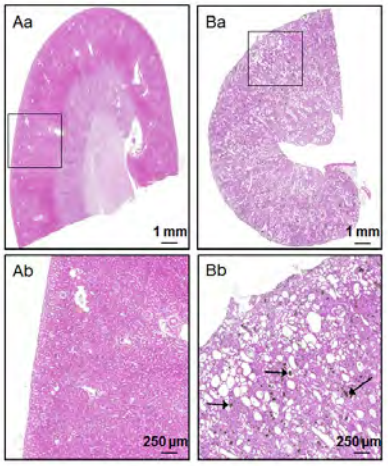

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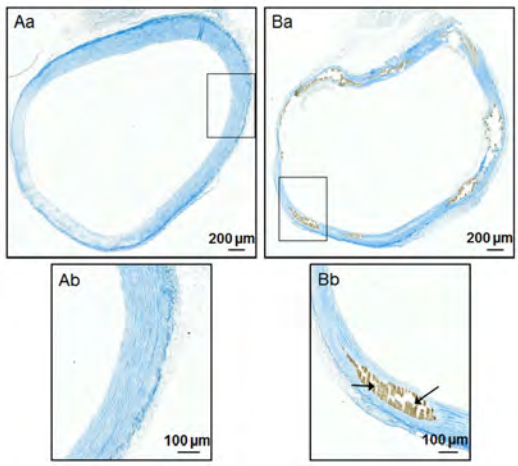

2

PROJECT EXAMPLES

Establishing a model for chronic kidney disease (CKD)

Chronic Kidney Disease (CKD) is the progressive, non-reversible loss of glomerular functional units of the kidney. Worldwide ≥ 2 million humans (2011) are kept alive through kidney replacement therapies, which represents only 10 percent of all final CKD patients whose organs need to be replaced. Consequently, preventing or delaying the CKD progression from stage G I-G IV/A I-A II to the final stage G V and A III by drug or dietary therapies is relevant worldwide from a medical and economic perspective. The efficacy and safety of these drug or dietary therapies has to be tested preclinically in in vivo models. Our group established such an in vivo model for a lethal or moderate CKD.

We injected different concentrations of adenine into six-month-old WISTAR rats for several weeks. This injection model is less stressful to the individual animal than other models regarding the indication CKD. The rats used are adult and are held for a relatively long time in our animal house. Therefore, we invested in better housing conditions for the animals and got a two-floor cage system appropriate for large, adult rats.

In the model, we could induce several pathological changes similar to the ones in patients with CKD. Dependent on the adenine concentration, we were able to induce symptoms indicating a final, lethal CKD or symptoms indicating a moderate kidney disease similar CKD stadium 3 in patients. In this context, we could develop new imaging techniques (see page 47) as well as test first diets.

From now on, this established model will be available to test different therapeutical approaches to help CKD patients worldwide.

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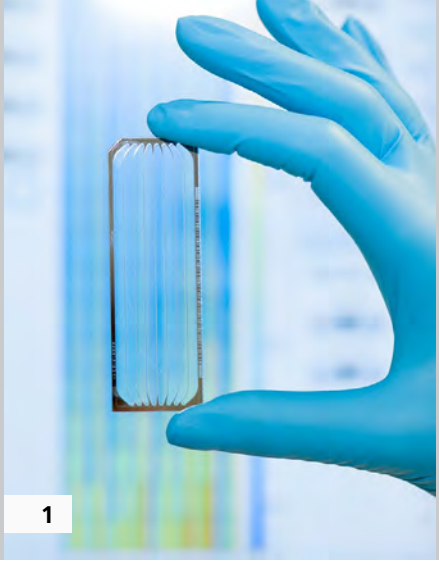
1 *Histological HE stain to provide an overview of the kidneys. Aa and Ab healthy animals. Ba and Bb animals with induced CKD.*

2 *Von Kossa stain on aorta cross-sections. Aa and Ab healthy animals. Ba and Bb animals with induced CKD.*



1

2

Development of novel biomarkers to diagnose and predict prostate cancer

The changing demographic landscape is causing a steady rise in the number of oncological, chronic-inflammatory and degenerative diseases. Despite a similarly growing number of therapeutic options, treating these diseases often proves unsatisfactory. Personalized therapy can bring about fundamental progress here. For this to work, the molecular basis of a disease first needs to be precisely determined and the case-specific disease progression and response to therapy has to be predicted. Ever since the human genome was sequenced in full in 2001, the decoding of disease-relevant genes has opened up new options for developing tailor-made approaches to therapy. Alongside evidence of changes in DNA patterns (e.g. mutations), the investigation of RNA gene expression patterns by means of transcriptome-wide sequencing is increasingly shifting into focus.

As part of the RIBOLUTION project, funded by the Fraunhofer Future Foundation, new biomarkers were identified for prostate cancer based on transcriptome-wide (RNA) sequencing together with microarray analyses. Biomarkers were identified here that can diagnose the disease and also predict the aggressiveness of the cancer.

In order to validate and subsequently use these biomarkers for diagnostic purposes, a manageable number of biomarkers is to be identified using a simple test. To do this, the RNA Biomarker Unit has come up with a workflow for detecting diagnostic biomarkers in the urine, using quantitative real-time PCR (qPCR). For optimization purposes, suitable reference and target regions as well as primers and probes were tested in depth and the reaction conditions were adapted, among other things. For the assessment, the selected biomarkers were investigated in close cooperation with the Bioinformatics Unit using a specially developed algorithm.

For the more complicated issue of predicting the cancer, the Next-Generation Diagnostics Unit developed a workflow based on RNA sequencing from FFPE biopsy material. The aim here was to identify a broad spectrum of potential biomarkers in clinically available samples. In the interests of reducing time and costs, sequencing was optimized in terms of sensitivity and robustness. Based on this established method, the transcriptome-wide sequencing of a large patient cohort (n>150) is currently being carried out to validate the identified biomarkers.

The workflows developed in this project are to be transferred to other indications in the future.

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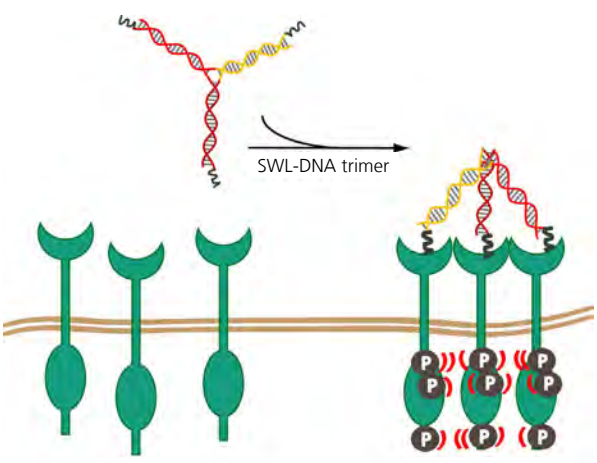
1 *Flow Cell for high-throughput sequencing.*
2 *Semi-automated extraction of nucleic acids (RNA and DNA).*



1

Pinpointed stimulation of EphA2 receptors via DNA-templated oligovalence

The field of DNA nanotechnology utilizes DNA strands not for their genetic encoding capabilities, but rather as construction materials. Using rational design principles, individual DNA strands can be assembled into precise nanostructures of nearly any shape. These nanostructures allow functional molecules such as peptides to be attached to nearly any unique location on their structure. Since structural features can be altered with the spatial resolution of a single base pair (0.34 nanometers), several molecules can be attached in closely controlled geometry. When these molecules are ligands that bind to specific targets, their spatial arrangement can be controlled according to the desired target's geometry. This results in optimized binding and/or signaling interactions.

In this project, the efficacy of SWL, an ephrin-mimicking peptide that binds specifically to EphrinA2 (EphA2) receptors, was enhanced by a factor of nearly four orders of magnitude by presenting three of these peptides on small DNA nanostructures in an oligovalent manner. Ephrin signaling pathways are critical in the development and progression of many types of cancer, and are potential targets in cancer diagnosis, imaging and treatment.

Here, the impact of SWL valency on binding affinity, phosphorylation (a key player for activation) and the regulation of phenotype prostate cancer cells that express EphA2 was quantitatively demonstrated. DNA structures with three SWL peptides significantly enhanced EphA2 phosphorylation by 8000-fold. Furthermore, the pinpointed interaction of these constructs showed an enhanced impact on the retraction of cells compared to one of EphA2's natural ligands – ephrin-A1. These results demonstrated that simple DNA structures can be used to greatly enhance the potency of otherwise weak signaling peptides, using principles of a nanometer-scale oligovalent arrangement.

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1 *Receptor clusters are formed by the peptide-coupled DNA trimers binding to EphA2 receptors (green). This leads to the autophosphorylation and activation of tumor-suppressing signaling pathways.*

Prognostic biomarkers for prostate cancer

Prostate cancer is the most prevalent cancer disease and the third most common cancer-related cause of death in European men [1]. Clinical behavior of localized prostate cancer is highly variable. Some men have aggressive cancer leading to death but many others have indolent cancers that are cured with initial therapy or may be safely observed. Patients often face unnecessary surgery because clinical and histopathological risk factors, as well as biomarkers and their according classification models, lack discrimination accuracy. Hence, there is a high clinical demand of biomarkers for the early prognosis of prostate cancer.

To address this, we strive for a better understanding of the molecular dysregulation in PCa. We conducted whole-transcriptome variation studies to detect gene signatures of prognostic value comprising protein and non-protein coding genes in fresh frozen radical prostatectomy samples and confirmed them in routine clinical materials of formalin-fixed and paraffin-embedded (FFPE) radical prostatectomy or biopsy samples.

We assessed the transcriptional landscape of more than two hundred tissue specimens of prostate cancer patients with long-term clinical follow up. For an unbiased assessment of transcriptional changes, we used analytical methods like custom expression microarrays and transcriptome-wide next-generation sequencing. We applied survival models to the expression values of each gene and combined evidence from different types of samples via a statistical meta-analysis. We combined all selected genes in a gene expression prognostic score per patient. The combined score showed a strong prognostic effect and correlates with time to death because of the disease. We could confirm the prognostic score in an independent testing cohort of a representative sample size and showed that the score also correlates with time to biochemical recurrence.

We developed a transcriptome-based score that predicts aggressive types of prostate cancer in cohorts of prostate cancer patients treated by radical prostatectomy. We further confirmed the score in an independent cohort of tissue specimens. The score is suitable to support treatment stratification and clinical decision-making for patients diagnosed with prostate cancer. We are currently confirming the score in tissue specimens that represent hands-on clinical material.

References

[1] https://ecis.jrc.ec.europa.eu/

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DEPARTMENT OF EXTRACORPOREAL IMMUNOMODULATION

Cellular adsorbers
Dialysis techniques
Organ-supporting technologies

THE DEPARTMENT AT A GLANCE

The department focuses on the development and evaluation of extracorporeal (outside the body), organsupporting technologies with a particular emphasis on supporting the immune system. We offer the full range of preclinical and clinical analyses of extracorporeal technologies based on a broad spectrum of in vitro simulations, animal models, as well as a powerful clinical study network for in and out-patients. Moreover, we offer self-developed unique analytic and diagnostic devices including an ex situ intestinal model, a cell sensor and novel protein assays.

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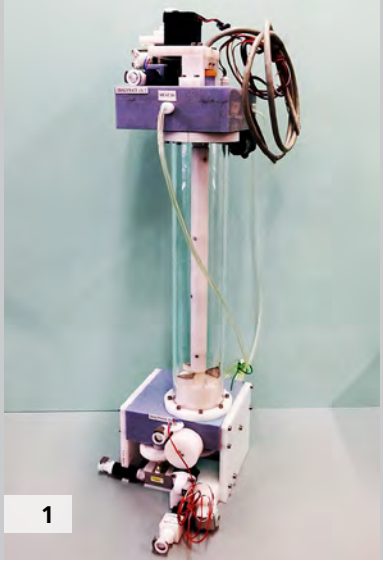

1

PROJECT EXAMPLE

Cryoregeneration of dialysate

Patients whose bodies have a weakened detoxification function due to a late-stage chronic kidney disease regularly need to have dialysis. The principle behind this procedure has been established for decades and is based on extracting water-soluble toxins (uremia toxins) in an extracorporeal filter, i.e. the dialyzer. The toxins pass from the blood into the purifying dialysis water (dialysate) via a membrane in the dialyzer. Around 120 liters of dialysate are required for every dialysis treatment, which usually takes four hours and is repeated three times a week. This water is taken from reverse osmosis (RO) plants in hospitals and specialized dialysis practices. Not only do these plants take up a lot of space and energy, but the water can only be used once as it disappears as waste water following dialysis. Based on a one-year time frame and 90 000 patients in Germany, over 1.7 million cubic meters of highly purified water are needed, without even taking the lost RO water into account.

Based on an approach which has never been applied to dialysis in the past, a procedure is being developed in the Department of Extracorporeal Immunomodulation that facilitates the regeneration of used dialysis water and could therefore completely change the huge problem of water dependability affecting the use of dialysis today. This procedure draws on the concept of freeze concentration used in the beverage industry and is based on the principle that the crystal lattice structure of frozen water excludes any previously dissolved foreign substances. As part of an automatable cycle, the procedure enables contaminated dialysate to be separated into pure water and a small residual volume containing impurities. This residual volume may arise from the patient's regular liquid intake, removing the dialysis' dependency on a pure water supply and making entirely mobile solutions conceivable. The fact that this separation occurs regardless of substance properties such as solubility, polarity, size, density, etc. is hugely beneficial compared with all conventional filter-based procedures, which do not demonstrate a sufficient filter capacity, especially for urea.

The procedure is currently being patented and an automated solution is undergoing development. This technical solution will then be used to carry out extensive investigations to specify process parameters that can later be used when working towards the initial clinical application. Notable industrial companies have already shown an interest in the procedure despite it's early stage of development.

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1 *The wash column is central to automating the cryoprocedure.*

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DEPARTMENT OF DRUG DESIGN AND TARGET VALIDATION

Medicinal chemistry
Assay and model development
Neurodegenerative diseases
Pharmacology
Drug development
Drug design (in silico)
Drug testing (preclinical)
Synthesis

THE DEPARTMENT AT A GLANCE

The Department of Drug Design and Target Validation in Halle (Saale) boasts considerable expertise in various areas of preclinical drug development, placing a special focus on neurodegenerative and inflammatory diseases. The department's work covers almost the entire range of activities associated with the early stages of drug development, from identifying and characterizing target proteins to identifying initial drug candidates right over to testing substances in the animal model. Members of staff at the Halle (Saale) branch are characterized by their extensive experience in industrial and pharma-relevant research. This allows scientific issues to be tackled on behalf of industry partners on the one hand, and new drugs and target proteins from the institute's own preliminary research to be identified, patented and subsequently form the basis of industry cooperations on the other.

Small molecules and biologicals will be developed and tested on the back of the department's new treatment concepts. Alongside this, testing procedures will be developed for the identification and diagnostic application of biomarkers, which allow the course of both the disease and therapy to be monitored. Furthermore, the department also houses the expertise required to create pharmacologically relevant in vitro and in vivo models.

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Besides modern peptide synthesis and protein analytics methods (MALDI-TOF and LC-MS), the department has also developed a broad spectrum of biophysical methods for characterizing therapeutically relevant metabolic pathways, whose key proteins as well as cell-based and pharmacological models are used to characterize innovative chemical and biological agents.

UNITS

Molecular Biotechnology Unit

The Molecular Biotechnology Unit develops and establishes analysis and model systems for use in cellular and molecular biology. This involves cell-based assays, gene expression analyses, immunological and protein-chemistry methods, sophisticated cell culture models and animal experiment approaches. In the area of preclinical development, the unit is able to conduct a series of cell-based tests to characterize substances with regard to efficacy, toxicology and transport. Furthermore, in collaboration with the department's analytical laboratory, pharmacokinetic parameters are determined in vivo and the effectiveness of small molecules and protein drugs are investigated in respective disease models. The unit is also able to establish new animal models to investigate enzyme functions in the organism. Beyond this, it assists with drug development in terms of regulatory preclinical practice.

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Protein and Drug Biochemistry Unit

The Protein and Drug Biochemistry Unit has extensive experience in the purification of target proteins and their enzymatic characterization. Besides traditional protein chromatography procedures, protein chemical methods are also used, e.g. spectroscopic and crystallographic methods for analyzing structure and enzyme-kinetic effect. The unit specializes in the humanization of antibodies to manufacture protein drugs right up to their semi-preparative extraction. The subsequent structure-activity analysis and structure-based molecular optimization round off the unit's portfolio.

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Drug Design and Analytical Chemistry Unit

The service portfolio offered by the Drug Design and Analytical Chemistry Unit covers the entire spectrum of medicinal chemistry and analytics required to identify potential new drug candidates from the field of "small molecules" and develop them into clinical candidates.

By using computational procedures, potential new target molecules are first designed in silico and evaluated as to their efficacy on the target protein. Once this stage is complete, synthesis and real testing on the isolated target protein can then be carried out. The unit is also able to provide analytical assistance to drug development in preclinical and clinical trials. Respective parameters can be pursued using HPLC-coupled mass-spectrometry methods. These investigations can also be conducted in line with regulatory requirements (GLP). Moreover, biophysical methods such as isothermal titration calorimetry and surface plasmon resonance spectroscopy are drawn upon to characterize binding behavior. Biological assays are developed and validated together with the other units, allowing the success of new types of treatment to be monitored using biomarkers.

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Protein Misfolding Diseases Unit

More than 300 000 new cases of amyloidoses are recorded in Germany every year. The diseases are caused by abnormally modified proteins being deposited in the body, usually in intercellular spaces. These insoluble protein fibrils, referred to as amyloids, damage not only the nervous system but also internal organs such as the heart, liver, kidneys, spleen or gastrointestinal tract and, in severe cases, also lead to their loss of function.

The Protein Misfolding Diseases unit carries out research into the impact of protein post-translational modifications and their influence on the emergence and prevention of amyloid diseases. To be able to detect pathogenic modifications using immunological assays, amyloid proteins are first expressed, purified and made to aggregate in vitro. Monoclonal antibodies are then produced and tested as therapeutic agents. The aim here is to develop personalized treatments in the form of antibodies.

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1

PROJECT EXAMPLES

Antibodies for the treatment of neurodegenerative diseases

Neurodegenerative diseases are characterized by the progressive loss of brain substance. The degeneration of nerve cells coincides with the development of dementia, i.e. a qualitative and quantitative decline of brain cognitive performance. Due to the rise of life expectancy, dementia, especially Alzheimer's Disease (AD), will pose a major challenge to our health systems in the decades to come. Despite the fact that some medication is available to relieve the symptoms of such diseases, no curative therapy is currently available.

The majority of neurodegenerative diseases is caused by a misfolding of proteins. This structural modification results in an aggregation that damages the surrounding tissue and nerve cells causing them to die off. An effective therapy has to prevent the peptides from aggregation and / or to accelerate the decomposition of these proteins. One way of triggering the degradation of the misfolded proteins is to apply antibodies which specifically target these non-natural proteins. The antibodies and misfolded amyloid peptides form complexes which are recognized and degraded by immune cells. One key aim of such approaches is to identify antibodies which only bind to misfolded, toxic material and which do not display any side activity to bind physiologically active peptides or proteins.

Therefore, our research focuses on so-called posttranslational modifications that are causally related to the development of the disease. Such modifications include, for instance, nitration, phosphorylation and the formation of isoaspartate. The project aims to generate and test antibodies which are highly specific to modified amyloid peptides. The most promising candidates will be selected from several different molecules and prepared for human use.

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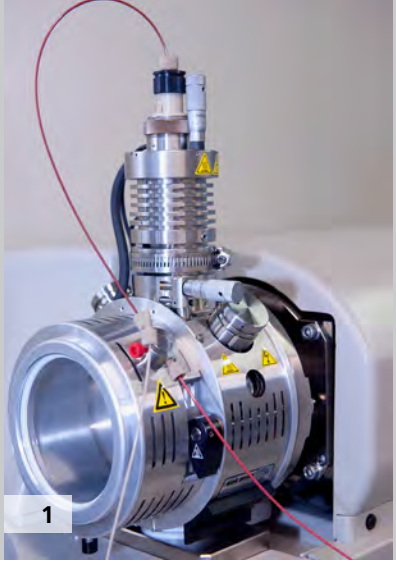
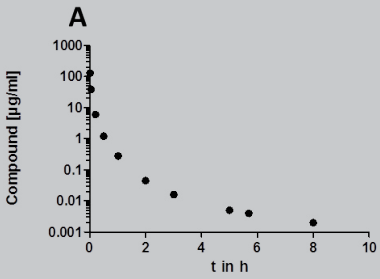
1 *Photo © GordonGrand – Fotolia.com*





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Determination of pharmacokinetic parameters of small molecules

A comprehensive characterization of physico-chemical, cell-biological and pharmacokinetic properties of small molecules are prerequisite for their preclinical development. This process is required for the application of efficacious, safe and well-tolerated molecules in human subjects later during clinical development. Important steps during preclinics are investigations on liberation, absorption, distribution, metabolism and excretion (L-ADME parameters) in animal models. Here, information on exposure, bioavailability and terminal half-life will be collected. These data serve as decision points for selecting preclinical candidates or are used for optimization, e.g. bioavailability of an already selected candidate, by formulation development.

The Department of Drug Design and Target Validation at Fraunhofer IZI develops new molecular therapies for neurodegenerative and inflammatory disorders. The department's strategy includes identifying novel drug target and testing novel therapies. For characterizing new small molecule classes, a catheter-based rat model for analyzing pharmacokinetics of such compounds has been established by the Molecular Biotechnology unit. The model is comprised of surgical application of a catheter in the jugular vein (V. jugularis) and in the carotid artery (A. carotis communis), respectively. Using this method, it is possible to obtain complete compound profiles from a single animal, which avoids inter-individual variations, e.g. when using mice. In addition, a close collaboration with the Drug Design and Analytical Chemistry unit enables rapid determination of compounds concentrations in blood samples by LC-MS.

The applied method is being used successfully within the Department of Drug Design and Target Validation, e.g. for own projects, such as the development of novel inhibitors for alternative beta-secretases or the development of novel inhibitors for the treatment of periodontitis. It is also requested and used by partners from industry and academia.

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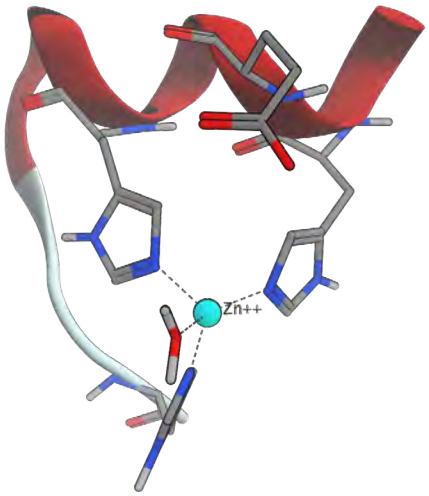
1 *Mass spectrometry analysis to determine the concentration of the active ingredient in the organism (A)*



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Broadening the chemical space of metal binding groups

A whole spectrum of target enzymes seen to be of medical interest contain a metal ion in their active site that is involved in the catalysis of the corresponding reaction. These metal ions usually present a starting point for the development of new drugs as the principal affinity of the respective inhibitor often emerges as the result of the medicinal substance binding to these metals. As however, until now, only very few active metal binding groups have been described in the literature, which then often do not block the actual target enzyme selectively but also other metal-dependent enzymes, the development of highly promising approaches often failed. Due to cross-reactivities within the enzyme class, matrix-metallo-protease inhibitors, for instance, were not pursued further despite years of intensive research.

A new computational chemistry approach has been developed in the Drug Design and Analytical Chemistry Unit that represents a combination of semi-empirical and quantum chemical methods alongside ligand- and structure-based approaches. Based on these complex calculations, it is now possible to significantly expand the chemical space of metal binding groups. Fragments discovered here are adapted for the respective application and constitute completely new chemical classes of molecules for future medicinal-chemical development. In the case of one particular metal-dependent acyltransferase, for example, alongside the four metal binders already known, another six new and just as active compound classes were able to be identified and pursued further.

As they had never been described in the past, they have now expanded the patent portfolio of the Department of Drug Design and Target Validation. The approach depicted here is currently being modified and adapted to the molecular properties of another target protein from the Astazine family. The aim is to avoid the possible adverse effects of potential new drugs described in the literature for the metal binding groups utilized so far.

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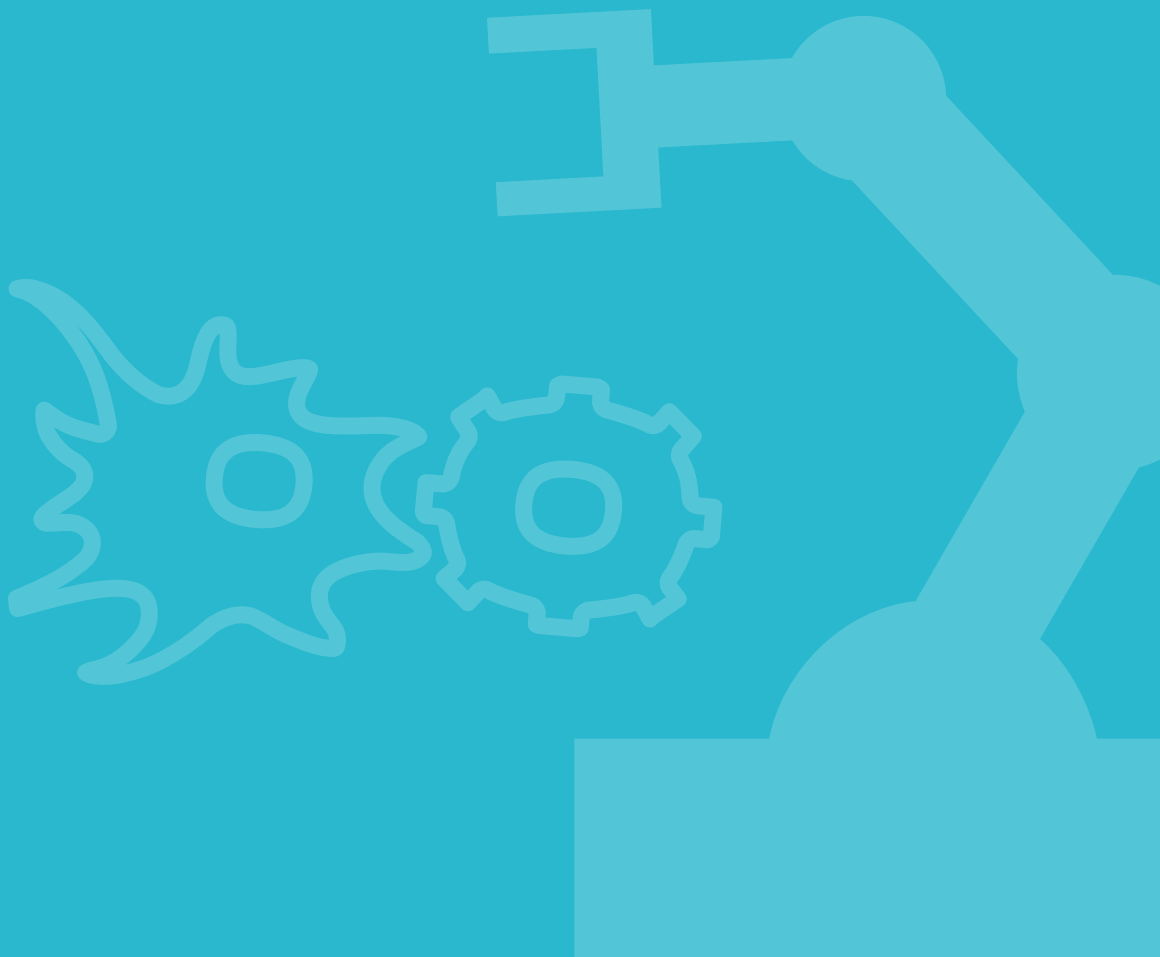
1 *View of the active site of Meprin β, a possible target enzyme involved in various fibrotic diseases. The graphic shows catalytically active zinc with the coordinating amino acids and a water molecule as the 4th ligand.*

Location Potsdam-Golm, Germany

DEPARTMENT BIOSYSTEM INTEGRATION AND PROCESS AUTOMATION

Point-of-care
In vitro diagnostics
Automation
Assay development
Device development
Process automation



THE DEPARTMENT AT A GLANCE

The department delivers solutions for complex laboratory automation tasks in biotechnology.

Work here focuses on processes related to bioanalysis, diagnostics and cell culture, expansion, preparation and monitoring and aims at increasing the efficiency, quantity and quality of laboratory processes including cell products.

A further focal area is found in developing procedures and devices for a broad range of point-of-care applications. Among other things, an in vitro diagnostics (ivD) platform is available for this purpose, which can be adapted to different diagnostic tests depending on the task at hand.

Furthermore, procedures and devices are also available for analyzing and using molecular interfaces and higher-order electronic effects. Special importance is also assigned to developing procedures to gently dehydrate and fix dry reagents, which are used in all variants in diagnostics and analytics.

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UNITS

ivD Platform Unit

The unit develops procedures and devices for various point-of-care applications. Based on miniaturized lab automation using microfluidics and biosensors, application-related, on-site solutions are developed for use in medical and non-medical fields. Among other things, an in vitro diagnostics platform (ivD platform) is available for this purpose, which can be adapted to different diagnostic tests depending on the matter at hand. Besides developing new diagnostic procedures, the unit offers customers and partners the opportunity to transfer existing tests (e.g. ELISAs, DNA microarrays, etc.) to the ivD platform. It also offers test optimization and technical verification, right through to authorization. The platform is open to numerous biomarkers and offers customers a fast way of moving from the biomarker to the actual product.

Current activities are focused around processing and detecting microbial samples (infection diagnostics, hygiene) and characterizing antibiotic resistances besides detecting specific nucleic acids in blood and other bodily fluids.

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Biomolecular Nanostructures and Measurement Technology Unit

The unit carries out research and development for the analysis of biomolecular interfaces and higher-order electronic effects. At the center of our activities are applications for point-of-care testing, however applications in a laboratory environment are also included. The methods used cover a broad range of microscopies including high-resolution optics, electronic and atomic forces microscopy, as well as THz spectroscopy.

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Biomimetic Functional Materials Unit

The unit develops technologies and solutions for fast immunoassays. Homogeneous assays with an affordable electrochemical readout system are one focus, but also innovations of mature technologies: A new surface chemistry was developed to minimize antibody and sample consumption in ELISA. "Smart" dry reagents tailored to the customer offer not only a high level of storage stability, but also added functionalities such as adhesion, transparency, slow-release kinetics or desiccation protection. Biomimetic electrochemical sensors, functionalized with artificial binding molecules (MIPs, "plastic antibodies"), offer new analytical options if antibodies are not available or desired.

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Laboratory and Process Automation Unit

This unit provides solutions for the automation of complex processes in biomedicine and biotechnology. The workflow in cell culture, cell expansion and monitoring, as usually done in the lab, forms the basis of analysis. The aim of all automation approaches is to standardize complex workflows and enhance efficiency as well as the quality of cell products.

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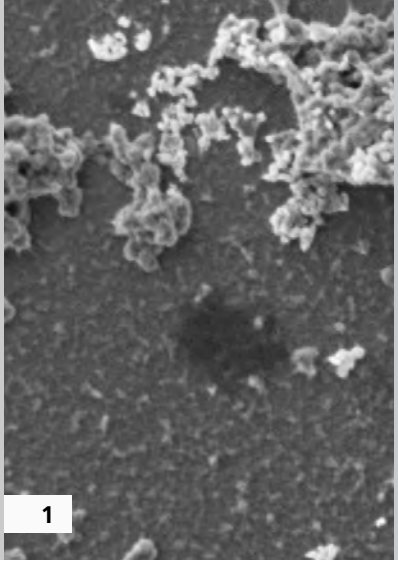

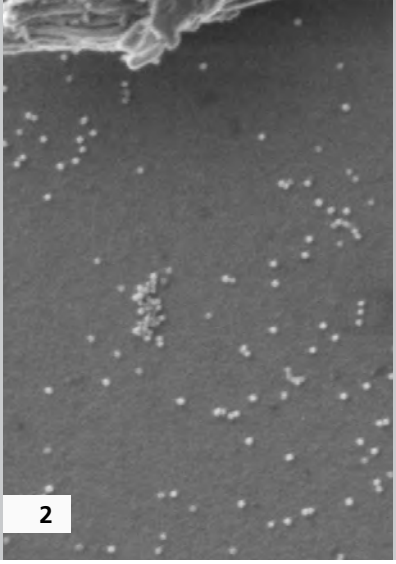

PROJECT EXAMPLE

Peptide-decorated biomimetic surfaces for influenza typing

The influenza virus has been the cause for annual flu epidemics and can lead to grave pandemic waves. The only efficient and cost-effective protection from flu is vaccination. For an effective vaccination recommendation by the WHO the circulating virus strains must be exactly analyzed (subtyped). In Germany this task is performed by the Robert Koch Institute in Berlin. The current best practice of virus analysis from patient samples comprises tedious animal experiments.

Based on short linear peptides as specific recognition elements and in cooperation with the Robert Koch Institute and the University of Potsdam, a new system for influenza subtyping is being developed. Peptides are synthetic molecules of nearly infinite chemical variety and can be tailor-made for every virus subtype. With a set of a few, highly selective peptides we want to devise a characteristic binding pattern, a "fingerprint", for each virus subtype. Unfortunately the binding interaction between proteins in the virus membrane and linear peptides are rather weak. Therefore we are developing a 3D-structured biomimetic surface that improves the visibility of this "fingerprint" by simultaneously binding several peptides to the same virus particle. Inorganic micro- and nanoparticles are immobilized on a gold surface as a hard template. Subsequent electropolymerization and finally the dissolution of the inorganic templates is used to produce thin polymer films with three-dimensional pores and cavities that can be decorated with specific, influenza recognizing peptides.

Binding of inactivated influenza A virus subtypes was investigated by electron microscopy (REM) and fluorescence imaging.

The ultimate goal is the safe discrimination of the relevant virus strains by an automated molecular test method without the need for animal experiments.

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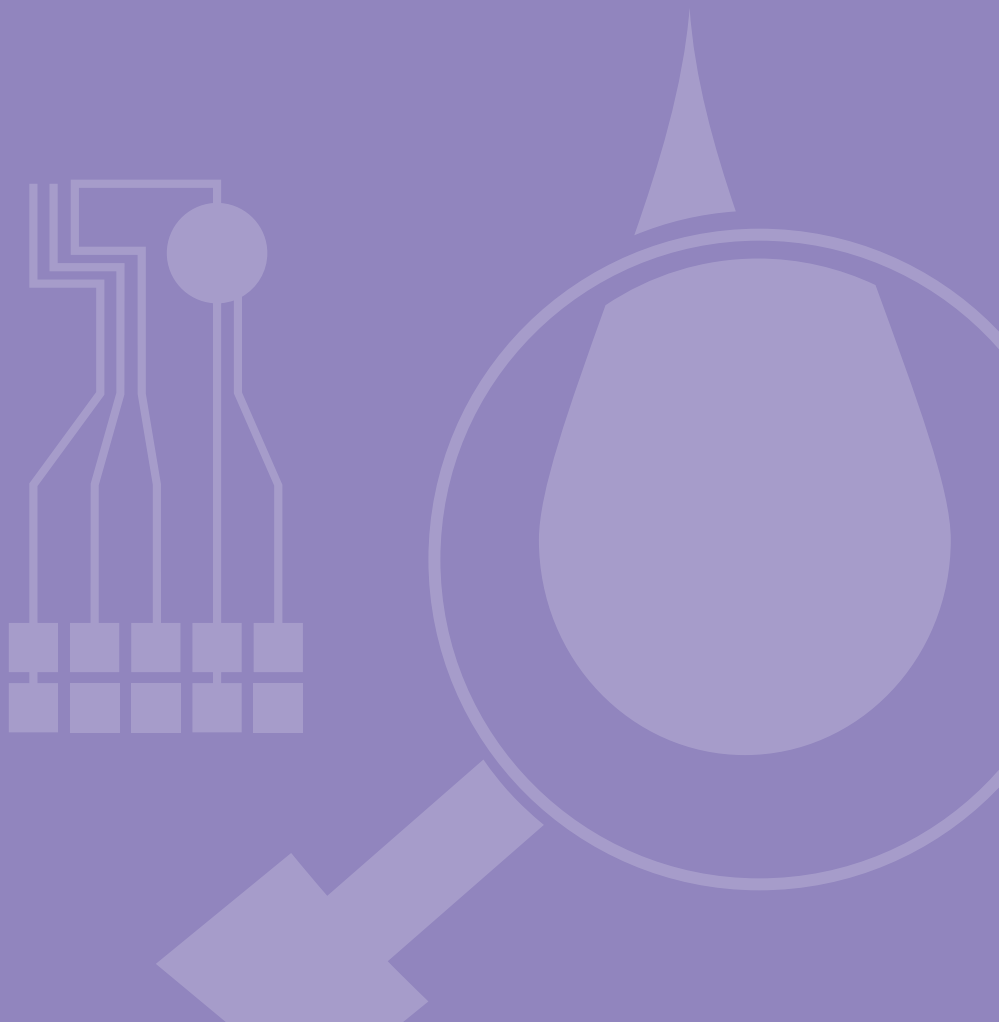
1 *Influenza A viruses (white balls, approx. 120 nm in size) bind to a peptide-decorated, porous PEDOT surface (REM).*
2 *Influenza A viruses (white balls, approx. 120 nm in size) bind to a peptide-decorated, planar PEDOT surface (REM).*

Location Potsdam-Golm, Germany

DEPARTMENT OF MOLECULAR AND CELLULAR BIOANALYTICS

Lab-on-chip
Microfluidics and systems
Biobanks
Rapid prototyping
Biosensor technology
Assay development
Functionalized surfaces



THE DEPARTMENT AT A GLANCE

The department is devoted to developing systems to detect, analyze and process challenging biological samples. These systems address demands in the fields of biomedicine, diagnostics, biotechnology, process control as well as environmental analytics, food safety and animal husbandry. The spectrum of solutions ranges from stand-alone sensor and fluidic components to integrated analysis systems and comprehensive database tools. The development of point-of-care tests, e.g. for drugs and serum screenings, forms as much a part of the unit's scope of activities as establishing assays for the validation of biomarkers. Lab-on-a-chip systems for cultivating, processing and analyzing cell samples present a further focus. These chips allow long-term cultivation and toxicity tests on suitable cell clusters and micro-precise positioning of single cells or sorting heterogeneous cell populations. All of the department's activities are based on its profound expertise in sensor technology, spotting and dispensing technologies, surface coatings, microfluidics and the integration of functional units into all-in-one solutions. Its competence in molecular and cell biology allows the department to use its technological abilities in the most purposeful manner. Work can be carried out efficiently using the state-of-the-art instruments and facilities available in the department's well-equipped laboratories.

By integrating biobanks into so-called metabiobanks, the department provides solutions that facilitate and support the web-based case-by-case and sample-by-sample search for human biospecimens and associated data across institutional and national borders.

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UNITS

Microarray and Biosensor Technology Unit

The unit develops and modifies the surfaces of biological materials with the aim of also analyzing and characterizing the smallest sample quantities in as much detail as possible. The technological implementation takes place both on geometric materials, such as fibers, and as well as on planar carriers, such as plates or chips. The surfaces themselves vary from glass containers and wafer materials through to plastics. The products developed by the unit include independent sensor elements (e.g. test strips) or analysis and database tools (cell and peptide chips) and can be applied to the various issues in the fields of environmental analysis, food control, herd management, process control and diagnostics.

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Biomarker Validation and Assay Development Unit

The group's activities include the development of specific assays for detecting and quantifying analytes in different matrices. The platforms used include microarrays, ELISA, lateral flow systems and bead-based assays for life science, environmental and food analysis. In addition, physic-chemical parameters such as kinetic constants (KD) can be determined and the composition or modification of surfaces can be characterized. All techniques are continuously being further developed for customer-specific applications. These applications include systems biology projects, the kinetic analysis of antibodies and the quantification of specific markers in serum samples.

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Molecular Bio-Engineering Unit

This unit converts natural biological processes into isolated artificial architectures and strategies which utilize new perspectives in applications of cellular structures, mechanisms and metabolisms. In former studies, for example, modified synthetic membrane proteins were used to fix extracellular entities. More recent studies deal with innovative immunodominant antigens taken from cDNA libraries of prokaryotic transcriptomes, which mainly consist of pathogens, besides the development and construction of antimicrobial peptides, especially synthetic and artificial peptides, within the scope of antibiotic resistances.

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Microsystems for In Vitro Cell Models Unit

This unit offers the application-related and customer-specific development of procedures and prototypes for cultivating, characterizing and processing precious cell samples. Our expertise in microreactors, microfluidics, sensor technology and functional polymer coatings forms the basis for innovative solutions, which are complemented by our knowledge in the fields of cell biology, toxicology and bioanalytics. The unit's interdisciplinary orientation enables us to provide well-founded, targeted advice and to address your specific needs. Our work focuses on (i) developing in vitro test procedures for the assessment of the toxicity of drugs and chemicals based on highly functional microbioreactors and relevant cell models, as well as (ii) establishing intelligent polymer coatings which allow the behaviour of adherent cells to be controlled on technical surfaces.

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Microfluidic Cell Processing and Cell Analytics Unit

This unit offers the application-related and customer-specific development of procedures and prototypes to process and manipulate demanding biological samples. It focuses in part on manipulating individual objects, e.g. the gentle and versatile handling and sorting of single cells and particularly small cell samples in microfluidic chips. This usually involves the use of electric fields in the radio frequency range. For more complicated tasks, this is combined with complementary manipulation procedures involving optical tweezers or microfluidic processes. In addition, the unit deals with the integration of sensor technology in microfluidic components to record key parameters relating to cells and other complex biological samples. In this area, the unit is developing powerful test systems for the assessment of blood compatibility of cardiovascular medical devices under highly-controlled flow conditions.

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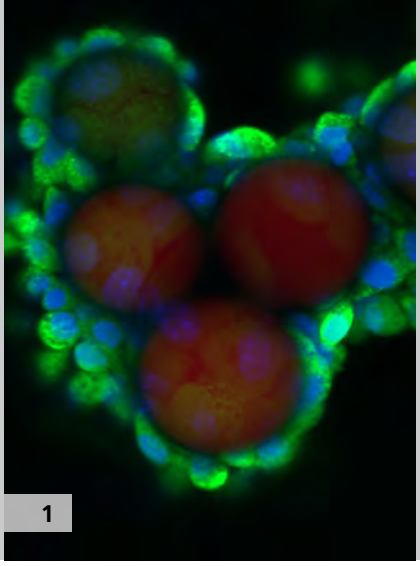

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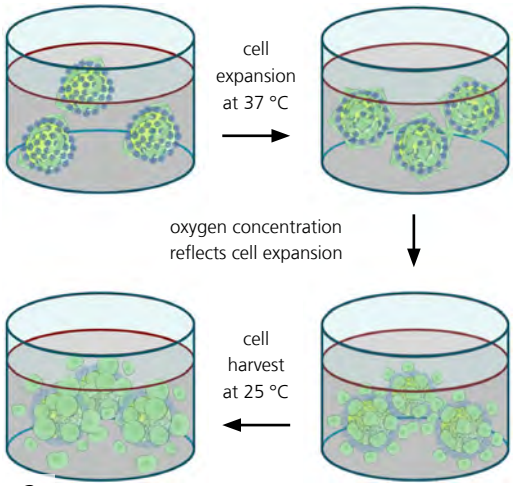

2

PROJECT EXAMPLES

Particle based sensors as substrates for the gentle expansion of cell samples

For establishing reliable in vitro test systems it is crucial to competently process and expand the cell material such that it is finally available at a high quality. In our view, the coating of particle-based mircosensors using thermoresponsive polymers is a promising approach in order to meet these requirements. The cultivation of adherent cells on microcarriers significantly increases productivity in respect to conventional cell cultures: Firstly, increased amounts of cells can be cultured with an increase of available surface. Secondly, the system enables a partial removal of cells and hence allows for continuous harvesting. In order to achieve this, particles are coated using thermoresponsive polymers. At 37 °C these polymers facilitate cell adhesion. Through a decrease of temperature below the phase transition temperature of 32 °C for a brief period, the polymers induce separation of cell surface contacts. In this state cells can be easily separated from the beads and harvested. In contrast to commonly used cell cultivation protocols, this procedure does not impair the viability of cells as it does not depend on highly invasive enzyme cocktails.

The integration of microsensor particles with an optical readout for the measurement of oxygen consumption in cell cultures enables the continuous monitoring of cell proliferation in a facile and robust fashion. The measured values correlate with the metabolism of the cells and hence provide crucial information on the vitality of the cells. This allows instant adjustment of the cultivation conditions, which ensures an economical use of usually expensive culture media while constantly maintaining high cell vitality. In this project such particles are used as microcarriers for the cells and hence simultaneously serve as cell substrate and as sensors. In addition, this combination has the advantage that the effect of compounds on cell vitality can be further monitored immediately after cultivation. We believe that our approach may have a substantial impact on the generation of meaningful cell models which are increasingly being used in toxicology or for drug testing through the reduction of costs and by increasing the quality of in vitro cell tests.

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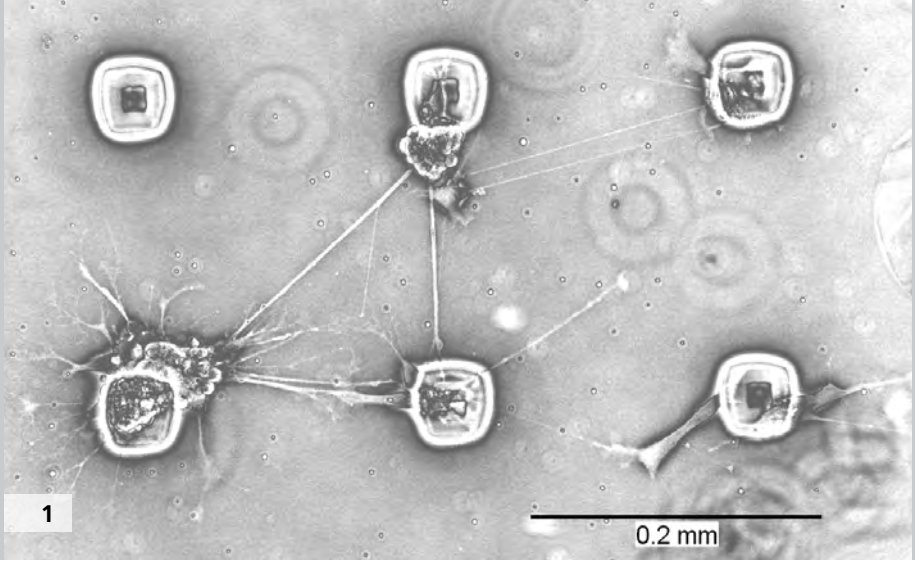
1 *CLSM fluorescence image of L929 mouse fibroblasts on 50 µm seized oxygen sensor particles after four days of cultivation.*
2 *Cultivation of adherent cells on micosensor particles coated with thermoresponsive polymers.*



Microstructured cell culture substrates for controlling neuronal cell growth in vitro

The analysis of artificial neuronal networks is raising great expectations with regard to the understanding of neuronal information processing and for the establishment of in vitro neuro-pharmacological test systems. In order to reproduce the highly organized architecture of neuronal tissue from dissociated neuronal cells in vitro, not only the position but also the direction of synaptic transmission between the individual cells in such networks has to be precisely controlled. However, despite strong efforts of numerous work groups worldwide this has not yet been satisfactorily managed. The aim of the present project is to investigate whether microstructured surface coatings of thermoresponsive polymers (TRP) can be used for creating neuronal networks with defined connectivity patterns. TRP coatings undergo a phase transition from a cell-repellent into a cell-friendly state in a temperature-dependent manner, which could allow for the elegant activation or deactivation of defined pathways for neurite outgrowth. With microfabrication techniques we will develop a TRP-coated cell cultivation substrate with integrated micro heating elements that will allow us to spatially control the surface temperature in the µm-range. The possibility of dynamically and spatially controlling the substrate's cell adhesive properties will form the basis for a 3-step cell assay for (1) controlling the cell position on the substrate, (2) controlling cell polarization by controlling the direction for outgrowing neurites and (3) after this, allowing neighboring polarized cells to contact each other and form functional synapses. For the evaluation and optimization of the neurocompatibility of our TRP coatings and cell cultivation protocols we will conduct cell biological as well as immunocytochemical analyses. The creation of neuronal networks of defined connectivity pattern will enable new methodological approaches to important neurobiological questions for example in the context of long-term potentiation (LTP) in basic science or pharmaceutical drug development for Alzheimer's or Parkinson's disease.

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1 *Neural network on a cell culture substrate with a micropatterned coating comprising thermoresponsive polymers. The position of the cell bodies is predefined by the geometric structure of the surface coating. The neurites, which connect the individual groups of cells to one another, are clearly recognizable.*

Location Potsdam-Golm, Germany

DEPARTMENT OF CELL-FREE AND CELL-BASED BIOPRODUCTION

Cell-free protein synthesis
Interaction assays
Protein characterization
“On-chip” synthesis
Antibodies and membrane proteins
Massproduction of algae
Biosynthesis of toxic proteins
Photo bioreactors
Cryophilic algae collection
Functional nucleic acids

THE DEPARTMENT AT A GLANCE

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Conserving resources and creating efficient material cycles are two challenges currently facing the economy and technology. The sufficient and affordable availability of high-quality synthetic products is an important basis for making progress here, especially in the field of health care. Active agents and analytes, biomolecules such as enzymes, antibodies and aptamers often form the basis of drug development in terms of diagnostics and therapy. But also in food and environmental technology, in the agricultural, cosmetics and detergent industries, the need for synthetic biomolecules is constantly on the rise. At present, many of these substances are manufactured using living cells and organisms. However, this is subject to considerable limitations. A sizable material and energy input has to be made to preserve cell metabolism itself. Beyond this, many metabolites, by-products and proteins, also in higher concentrations, are toxic to cells or organisms and can impede or even prevent these substances from being manufactured cost-effectively.

The cell-free bioproduction of high-quality proteinogenic biomolecules opens up completely new possibilities here. By using only the subcellular components of the organisms required for synthesis it is possible, in suitable reaction environments, to efficiently manufacture biomolecules with complex and also completely new properties. The technologies established at the Potsdam-Golm site allow these procedures to be used in an economically efficient way, thus creating a new basis for the economic production of active proteins.

The development, synthesis and also transfer of functional nucleic acids such as aptamers into market-relevant applications are just as much a focus as the analysis of cold-adapted snow algae in extremophile research. The latter of these are being used to extract high-quality substances such as antioxidants or fatty acids and are being manufactured in photobioreactors. The CCCryo culture collection is a unique bioresource that can be used by interested academic and private enterprise groups.

UNITS

Functional Nucleic Acids – Aptamers Unit

The Functional Nucleic Acids – Aptamers Unit aims at developing new innovative products on the basis of aptamers. This goal comprises the generation, synthesis and functionalization of aptamers as well as the integration in diverse applications. The unit thereby seeks a close collaboration with the industry and academic institutes. Primarily, aptamers are short, single-stranded DNA and RNA molecules with the particular feature of binding high-affine and high-specific a target molecule such as antibodies. The very broad capabilities of aptamers as binding molecules are used in analytical, diagnostic and therapeutic applications. A focus is on the generation of new aptamers by using an automatic in vitro selection process as well as a monitoring and managing process. Additionally, the unit develops of aptamer-based detection methods such as lateral flow assays or so-called aptasensors.

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Eukaryotic Lysates Unit

The unit is developing cultivation systems for eukaryotic cell lines in order to obtain translationally active lysates for cell-free protein synthesis. In this respect, testing new cell lines for their in vitro expression capabilities is of highest interest. Furthermore, the unit develops and optimizes eukaryotic cell-free translation systems. The influence of fermentation conditions, cell disruption as well as transcription and translation components are of special interest for the translational productivity of the generated lysates.

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Extremophile Research & Biobank CCCryo Unit

The unit studies the adaptation strategies and industrial usability of cryophilic (= cold-loving) freshwater microalgae. The aim is to characterize these so-called snow and permafrost algae with regard to the various strategies by which they oppose extreme environmental parameters such as cold, UV radiation, drought and osmotic stress, before transferring these natural adaptation strategies into industrial applications. The CCCryo culture collection is unique in its diversity and scope and forms the basis of this work. Furthermore, the unit develops optimized photobioreactors for a sterile mass bioproduction of these autotrophic organisms on an industrial scale

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Cell-free Protein Synthesis Unit

The unit researches and develops systems for the cell-free synthesis of recombinant proteins. A special focus here lies on characterizing, modifying and examining the functions of cell-free manufactured proteins, with particular emphasis on ion channels, glycoproteins and antibody formats. Quick and affordable target-protein synthesis is ensured as only the constituents of the cells are used. The use of eukaryotic cell lysates also allows the synthesis of post-translationally modified proteins. Beyond this, position-specific labeling enables proteins to be specifically modified, changing and optimizing their properties, e.g. through the introduction of polymeric groups. By introducing fluorescent groups at selected positions, membrane proteins in particular can be measured, functionally characterized and analyzed with an eye to identifying new binding molecules.

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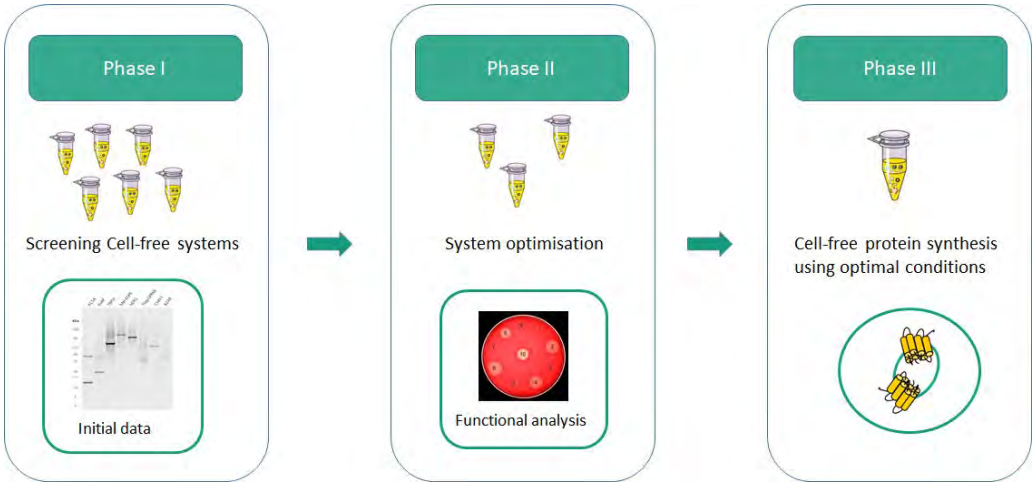

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PROJECT EXAMPLES

Evaluation of protein synthesis in cell-free systems

Cell-free protein synthesis, often referred to as in vitro translation, is a technique that can be carried out quickly and efficiently and leads to the goal with significantly fewer steps compared to in vivo methods. With this method, proteins can be synthesized directly in their natural environment using lysates derived from cultured cell lines. Various cell-free systems, based on lysates from prokaryotic and eukaryotic resources, enable the production of a broad spectrum of differently structured and modified proteins. In the course of the project, different cell-free systems will be investigated to find the appropriate system for each problem. Special requirements such as glycosylation, membrane protein synthesis in its native environment, disulfide bridge formation or signal sequence cleavage are addressed.

The evaluation can be divided into several phases. During the first phase, a first evaluation of the synthesis of the target protein is performed. In this phase, different lysates can be used to establish the optimal system for the expression of a specific target protein (based on cultured insect, CHO or human cell lines, *E. coli* and wheat germ lysates). Plasmids or mRNA can be used as templates. The testing of already existing templates or the design and generation of optimal templates is realized for the different systems. The introduction of mutations, e.g. for protein engineering, is also possible. A further optimization of the reaction conditions in defined systems can be carried out in the next project phase to improve the yield or activity of newly synthesized proteins. The purification of the target protein, the performance of activity assays (e.g. ELISAs), the electrophysiological characterization of membrane proteins (e.g. ion channels) but also cell culture assays (e.g. for activity studies) can be included in this evaluation phase. After the successful evaluation of the protein synthesis conditions, the target protein can then be synthesized in µg to mg scale and made available for further downstream applications.

In addition to the evaluation of the protein synthesis, templates such as mRNA or DNA can also be validated and the influence of the sequences as well as the quality of the template on the protein synthesis performance can be investigated. There are many applications and due to the individuality the evaluation of protein synthesis is an interesting option for industrial research projects.

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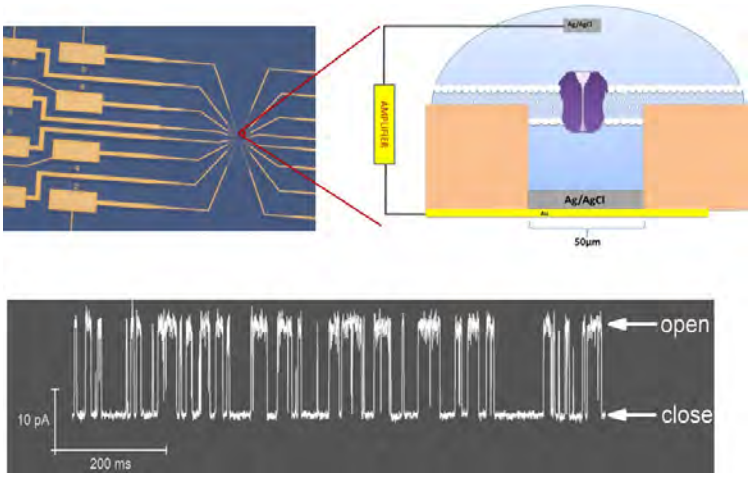
1 *Overview of the individual project stages for evaluating protein synthesis in cell-free systems.*



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Cell-free synthesis and functional analysis of membrane proteins

Membrane proteins represent more than two thirds of the known protein targets for drugs due to their involvement in vital cellular processes. Among them, ion channels and transporters have a crucial role in human physiology and any functional defect or overexpression of these proteins could affect the cellular activities which could often lead to a wide range of pathological conditions like channelopathies, metabolic disorders, cellular damage, and poor drug adsorption. Therefore, they are targeted by several marketed drugs and have a larger scope for the future development of new drugs. Synthesis of membrane proteins in vivo is challenging due to low yields, solubilization and purification problems, toxicity due to overexpression, and functional assessment. This method provides a complete openness with a high degree of controllability allowing the direct manipulation of the reaction conditions to influence protein folding, disulfide bond formation, incorporation of unnatural amino acids and the expression of toxic proteins. Eukaryotic lysates derived from *Spodoptera frugiperda* (Sf21) and Chinese hamster ovary (CHO) cells are used to synthesize the membrane protein of interest. The synthesized protein is incorporated directly into native endoplasmic reticulum (ER) derived microsomes during the cell-free synthesis. Microsomes harboring the active protein of interest were used for the functional analysis. In the case of prokaryotic cell-free systems, empty nanodiscs synthesized in-house are added directly into the reaction mixture. After the synthesis nanodiscs with incorporated membrane protein is purified and used for functional analysis. Thus the efficient use of cell-free protein synthesis helps in the economic production of functional membrane proteins as targets for drug development. Planar bilayer electrophysiology is used to study the ion channel activity by reconstituting them artificially into artificial lipid bilayers. Ion channels are analyzed by planar lipid bilayer electrophysiology on a multi-electrode array. Planar bilayer electrophysiology helps to monitor the ion channel activity after the reconstitution into an artificial planar bilayer individually at a molecular level without any interfaces.

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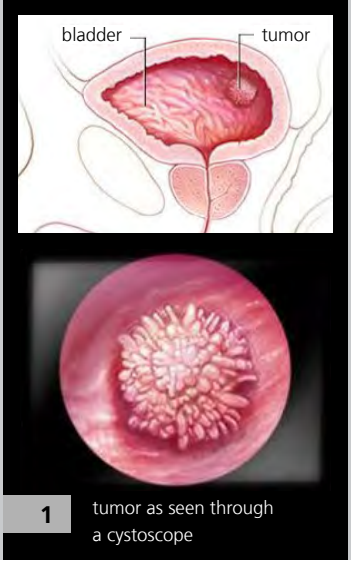
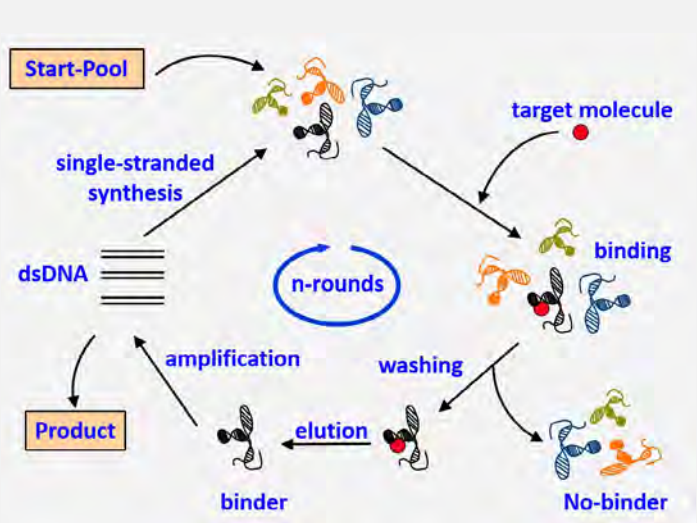
1 *Electrophysiological investigations on planar lipid bilayers are conducive to the functional characterization of cell-free synthesized ion channels.*



1 tumor as seen through a cystoscope



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ABBA: Aptamer-based biomarker assay for early diagnosis of bladder carcinoma

The societal need to be able to diagnose bladder cancer (BC) effectively and detect it at an early stage is especially apparent when considering the fact that BC counts among the most common newly diagnosed tumor diseases and causes of tumor-related death in the world as well as being one of the "most expensive" tumors in terms of diagnosis and therapy. At present, this form of cancer can only be reliably diagnosed on the back of an invasive procedure (cystoscopy with biopsy). This procedure is not only expensive but also uncomfortable and very laborious for the patient, hence only being used where there is reasonable suspicion. An early BC diagnosis would enable more efficient medical care and could also give identified cancer patients an increased chance of receiving curative treatment as therapy would start sooner. Especially in the case of high-risk patients, this could also cut some of the major costs involved in treatment and continuous therapy monitoring.

As part of the interdisciplinary "ABBA" project, tumor marker proteins (biomarkers) are to be detected quickly and reliably based on the development of aptamer-based biomarker assays. These diagnosis systems have to satisfy the high demands placed on sensitivity, accuracy and reliability, besides quickly evaluating the measurements and optimally adapting to established work processes. The desired biomarker assays are focused around aptamers as specific binding molecules for BC-marker proteins in the urine. To this end, new aptamers are being generated against its biomarkers with the introduction of NGS technology (high-throughput sequencing) at Fraunhofer IZI-BB; the newly developed methods are being evaluated based on strip tests and microtiter plate assays with an eye to sensitivity and specificity, as well as speed and cost in real urine samples.

The new biomarker assays are expected to help recognize cancer at an early stage and therefore help to determine what check-ups are necessary and what treatment measures may be required. They will also serve as a functional model for diagnosing biomarkers for other types of cancer in the future. The project is oriented, among other things, towards the increasing life expectancy of the population in industrialized countries, which goes hand in hand with rising costs for diagnosing and treating age-related diseases, especially tumor diseases.

Funded by:

EUROPÄISCHE UNION
Europäischer Fonds für Regionale Entwicklung

Investitionsbank des Landes Brandenburg ILB

LAND BRANDENBURG

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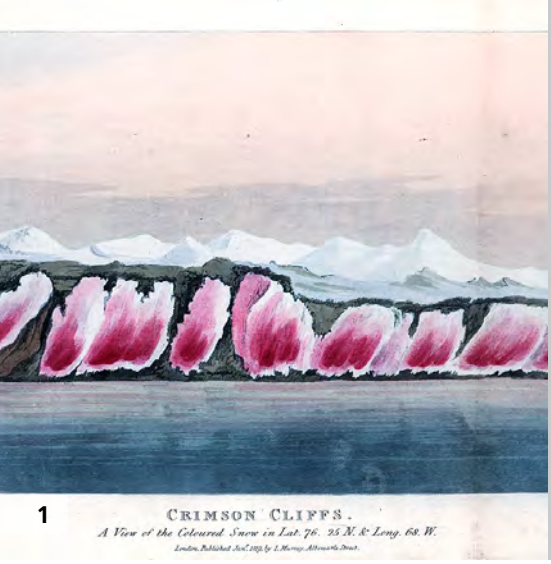
1 *Bladder cancer (source: https://newsnetwork.mayoclinic.org).*

2 *SELEX process for generating aptamers.*



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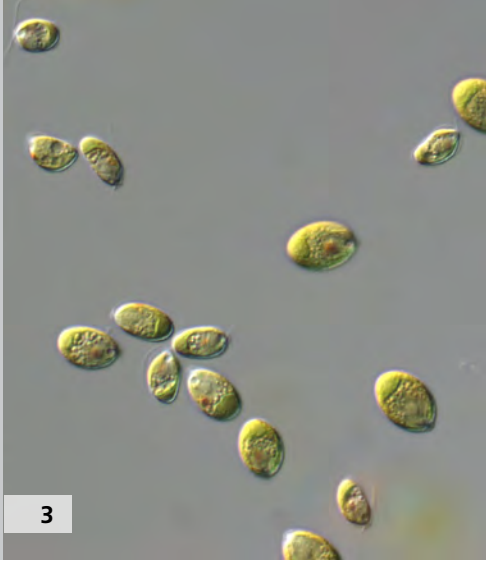

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From the alga of the year 2019 *Chlamydomonas nivalis* to the genome of cold-adapted snow algae

In 1819 Captain Sir John Ross brought home Red Snow from a polar voyage exploring the Northwest Passage. This striking phenomenon was observed by the seamen when sailing along the Crimson Cliffs in Baffin Bay on the north-western coast of Greenland. Initially the responsible organism could not be identified, however, soon one assumed a green alga was producing those carotenoid-rich red-colored resting stages making the otherwise white snow turn blood-red. Remarkably, until today the only known cell types of this species, *Chlamydomonas nivalis,* are the non-proliferating cysts, making this species uncultivable in the lab. Also, until today the correct taxonomic identity of this extremophilic alga, its biological name, has not been resolved yet. This enigmatic microalga has now been nominated the alga of the year 2019 by the Phycology Section in the German Society for Plant Sciences, 200 years after its first more detailed description. A manuscript for its taxonomic revision has just been submitted.

During the history of snow algae research, it has been shown that not only the red cysts, but also other cryophilic (cold-adapted) green-colored algae dwell well on the otherwise red-colored snow fields – and those indeed can be cultured and multiplied in the lab for detailed investigations. A comprehensive collection of these extremophilic algae, which were collected by our research group during expeditions to the Arctic and Antarctic, is being curated since 1999 in the biobank CCCryo (Culture Collection of Cryophilic Algae, www.cccryo.fraunhofer.de) at Fraunhofer IZI-BB. They are available to the international scientific and industrial community for research.

Currently, three special snow algal strains are being studied intensely on a genetic level in a comprehensive sequencing project. We want to understand how these approximately 20 µm small plants manage to thrive so well under such extreme environmental stress conditions such as cold and freeze, light and UV, salt and drought conditions. The genomes and transcriptomes of these 3 algal species are being investigated together with partners from the USA and Germany to identify special enzymes and other proteins as well as metabolites and pathways.

We clearly focus on industrially relevant enzymes for the food processing market (optimization for low temperatures and innovative processes), UV- and cold-protective cosmetic ingredients as well as special enzymes for diagnostic laboratory applications. Our recent results reveal extraordinarily large genomes in these extremophiles. The assembly and annotation are challenging, but we are underway to prepare the basis for future projects based on genomes from these interesting cryophiles.

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1 *Red snow along the Crimson Cliffs painted by Sir John Ross (engraved by Daniel Havell) during the expedition in 1819. Source: Courtesy John Carter Brown at Brown University, The Archive of Early American Images, CC BY-SA 4.0*

2 *Green snow produced by proliferating green snow algae on Makarov glacier in north-western Spitsbergen.*

3 *One of the three cryophilic (cold-loving) snow algal strains currently being sequenced.*

CENTRAL FACILITIES AND SERVICES

GLP TEST FACILITY

Good Laboratory Practice (GLP) describes a quality assurance system for conducting safety tests on chemicals, drugs, pesticides and food additives. It regulates the implementation, documentation, archiving and reporting of respective tests.

Fraunhofer IZI has been certified as a GLP test facility since 2009. The facility plans and conducts preclinical efficacy and safety studies for new drug candidates (especially ATMPs) and medical devices (ISO 10993) under GLP and GLP-analogous conditions. This involves developing and validating suitable in vitro and in vivo models. The test facility boasts a state-of-the-art setup for keeping small animals as well as small and large animal operating rooms. Furthermore, a broad spectrum of validated SOPs are implemented here for equipment and methods.

The test facility is currently certified for testing category 9. This includes, among other things, safety testing for ATMP immunotoxicity / immunogenicity, biodistribution and tumorigenicity in vitro and in vivo.

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GMP MANUFACTURING

GMP (Good Manufacturing Practice) describes a set of quality assurance guidelines for production processes and spaces with regard to drugs manufacturing. It regulates, among other things, the requirements concerning hygiene, facilities, equipment, documentation and controls.

Fraunhofer IZI assumes the manufacture of investigational medicinal products for clinical trials. Manufacturing capacities here range from therapeutic antibodies over to so-called advanced therapy medicinal products (ATMPs). These include cell-based drugs such as cell, gene and immune therapeutics as well as tissue engineering products.

Antibodies

In recent years, the increasing number of therapeutic monoclonal antibody (mAb) candidates under preclinical and clinical development have required new flexible, efficient, and economic opportunities for GMP production of therapeutic antibody candidates. Small-scale batch production of test samples for late preclinical GLP animal studies or for phase-1 and phase-2 clinical studies is often not appropriate for large-scale manufacturing facilities in the industry.

The clean rooms used for antibody production cover a total area of 180 m² and comprise all clean room categories from D to A. The use of single-use equipment and materials enables an easy adaption to new process requirements. The GMP facility can be used for different contract manufacturing processes for preclinical and clinical (Phase 1/2) test samples as well as for process or instrument validation projects under consideration of special customer requests. The standard equipment can be easily adapted for new products.

The manufacturing team's portfolio includes transferring biopharmaceutical candidates from preclinical research into clinical development, drafting user-specific processes and manufacturing e.g. human monoclonal antibodies on a 200 L scale in compliance with GMP.

In summary the main advantages are:

- High flexibility
- Easy switch to different products
- Fast implementation of technology changes
- Customized production
- Ideal batch size for preclinical and early clinical trials
- Possibility to obtain ready-to-use GMP-compliant products by integrated sample filling

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Advanced Therapy Medicinal Products (ATMPs)

The Fraunhofer IZI maintains three GMP-compliant clean room facilities. Through the flexible design, the facilities are especially attractive for new biotechnology companies that seek to bring newly developed medicinal products into clinical application via clinical trials. The facilities are divided into different independent suites. Each has its own grade C clean rooms (preparation), own air locks from grade C to B (personnel and materials transfer) and two grade B rooms (aseptic manufacturing). The clean room grade A is provided via laminar airflow cabinets that are installed in the B-rooms. The available clean room suites are specialized in conducting processes for manufacturing human autologous and / or allogeneic cell and gene therapeutic products (advanced therapy medicinal products). In addition to the clean rooms and the technical infrastructure, the Fraunhofer IZI offers assistance for the set-up and validation of GMP-compliant manufacturing processes as well as for obtaining a manufacturing authorization pursuant to section 13 of the German Drug Act (AMG).

Why are GLP and GMP important?

The clinical trial of new drug candidates is an essential step on the way to approval. Since the 12th revision of the "Arzneimittelgesetz AMG" (German Drug Act) every clinical drug trial must be approved of by the responsible higher federal authority ("Bundesinstitut für Arzneimittel und Medizinprodukte", Federal Institute for Drugs and Medical Devices, Paul-Ehrlich-Institut) and by the responsible ethics committee prior to the initiation of the clinical study. In order to obtain this authorization, the efficacy and safety of the investigational medicinal product must first be verified within the framework of GLP-compliant preclinical investigations (e.g. toxicological testing procedures). Furthermore, the quality of manufacture of the investigational medicinal products must be verified by a GMP manufacturing authorization pursuant to § 13 AMG. Relevant trial results from GLP-certified trial institutions and a GMP manufacturing authorization are thus absolutely prerequisite when applying for the clinical trial of a new medication.

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IMAGING

Phenotyping biological samples using multiple imaging methods forms a core competence of preclinical research. This enables thorough depiction, from the smallest structures (cell organelles) right through to entire organ systems, both in spatial and temporal resolution (4D).

Fraunhofer IZI has access to a comprehensive, state-of-the-art equipment pool that enables the acquisition and evaluation of various (also correlative) image data. Partners and customers are advised on biological, technical and economic matters and supported in carrying out and evaluating experiments. Furthermore, experimental procedures and equipment can be used, adapted and developed.

In vivo imaging

Magnetic resonance imaging (7 Tesla high-field small animal MRI) (image 1)

- Examination of soft tissues and organs, use of contrast agents and cell labeling possible, long-term measurements in single individuals
- Depiction of anatomical changes, MRS, diffusion methods, functional imaging

Computer tomography (CT and X-Ray for small animals) (image 2)

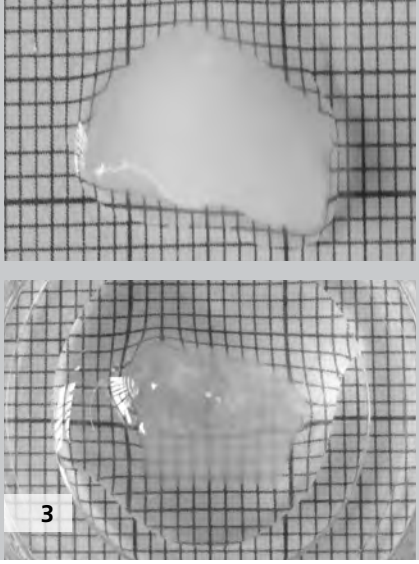
- Depiction of dense (bone, cartilage) and contrast-enhanced (soft tissue) structures
- 3D data sets can be used for conformal radiation treatment planning

Fluorescence and bioluminescence imaging for small animals

- Monitoring tumor growth and progression of inflammation, tracking cell movements following transplantation (cell tracking)
- Complex reconstruction of in vivo parameters by means of fluorescent imaging tomography (FLIT) or, in the case of bioluminescent sources, by means of diffuse light imaging tomography (DLIT) and spectral unmixing

Bedside imaging for small animals

- Various ultrasound units with a number of transducers and an implemented Color Doppler
- Flexible miniature cameras for the routine endoscopic examination of small animals and for the development of new lens attachments



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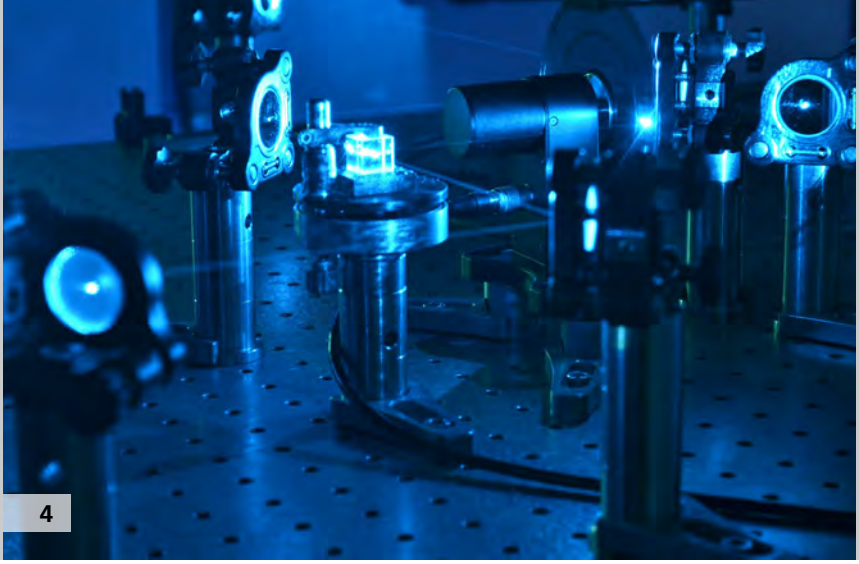

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In vitro / ex vivo imaging

Clearing tissue samples (image 3)

- Preparing samples for imaging (especially 3D fluorescence microscopy)
- Enabling detailed images of deeper layers of the sample that are usually only visible through histological sections

Confocal laser scanning microscope with live cell imaging

- Analysis of cell cultures and tissues in 4D, localizing target structures inside cells
- Standard laser lines from blue to red, water immersion lenses, real-time rendering and quantification of results

Light sheet microscopy (image 4)

- Flexible light sheet microscope with modular sample chamber for sample sizes from just a few µm to 2 cm
- For the study of light-sensitive live-cell samples in high temporal resolution

Atomic force microscopy

- Nanometer-scaled, micro-mechanical sampling of surfaces using a cantilever measuring needle and measurement of the occurring atomic forces

MALDI Mass Spectrometry Imaging (MALDI-MSI)

- Label-free methods of depicting the distribution of macro molecules in histological samples based on their degree of ionization and time of flight (TOF) in the electric field; special sample preparation and matrix application required, statistical evaluation of distribution patterns

Laser capture microdissection

- Isolating individual cells or tissue structures by means of microscopic laser cuts, analyzing samples using molecular biology methods (RT-PCR, proteomics)

Hardware-linked evaluation process

- Stereological quantification using the upright fluorescence and reflected-light microscope for unbiased histological evaluations
- Virtual microscopy in order to create completely virtual tissue sections for digital post-processing, high-throughput technique

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CENTER FOR EXPERIMENTAL MEDICINE

The development of new drugs entails testing using suitable animal models. Animal experiments are therefore an integral component in the development of new drugs, therapies and diagnostic procedures. The institute's Centre for Experimental Medicine (TEZ) is a central unit which facilitates important steps in translating research findings into a clinical application for human subjects.

Moreover, the institute has access to one of the most state-of-the-art animal houses in Germany. The TEZ is distinguished by its highly technical facilities, which are optimized to handle preclinical research projects. These facilities include modern rooms in which the animals are kept, featuring standardized hygiene levels and individually ventilated cage systems that are monitored via the building management system.

The health and care of the animals is of the highest priority. Highly qualified personnel support the scientific staff in daily care, health monitoring and breeding activities, and in administering treatments.

All experimental work can be carried out under practically sterile conditions. Several fully fitted operating suites allow small and large animals to be examined and treated. The comprehensive, state-of-the-art equipment guarantees correct anesthesia, analgesia and species-relevant blood analyses.

An expansive equipment pool for imaging technologies at the institute enables partly non-invasive analysis methods and also contributes towards reducing the need for animal experiments. This means, for example, that in vivo imaging analyses can be carried out using, for instance, 7 Tesla magnetic resonance imaging, bioluminescence imaging or small-animal CT.

In order to work on a range of issues, the TEZ has access to areas approved for genetic engineering safety levels S1 to S3; it may also conduct in vivo studies in line with GLP (Good Laboratory Practice).

The TEZ forms the central interface at the institute for processing preclinical development projects. Furthermore, cooperation projects with external clients and other research institutes are also carried out. At the same time, the TEZ acts as a training facility for animal care supervisors in a research and clinical setting, also offering advanced training courses for experimenters.

Adherence to the animal welfare guidelines is strictly monitored by the institute's animal welfare officers and regularly controlled by the regional animal welfare authority.

Equipment and services:

- Small animals are kept under state-of-the-art standards and permanently monitored
- Animal husbandry under GLP standards
- Animal husbandry with the option to use infecting agents for experimental infection

- Quarantine services
- Standard in-breeding and breeding transgenic lines
- Operation units in various areas including provision of inhalation anesthesia for small and large animals

- Large-animal OP area with intensive care capacity
- C-arm
- Option for individual stereotactic brain surgery
- Autopsy room for large animals
- Intraoperative blood gas analyses

- Small animal endoscope
- Blood cell meter
- Surgical microscope
- Stereotactic manipulation
- Temperature control during operations

- In vivo bioluminescence
- Small animal magnetic resonance imaging
- Small animal computer tomography
- X-ray unit for whole-body irradiation and pinpointed radiation therapy
- Large capacity autoclave
- Sterilization units using hydrogen peroxide fumigation
- Cryopreservation of spermatozoa and embryos
- Tissue bank

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RIBOLUTION BIOMARKER CENTER

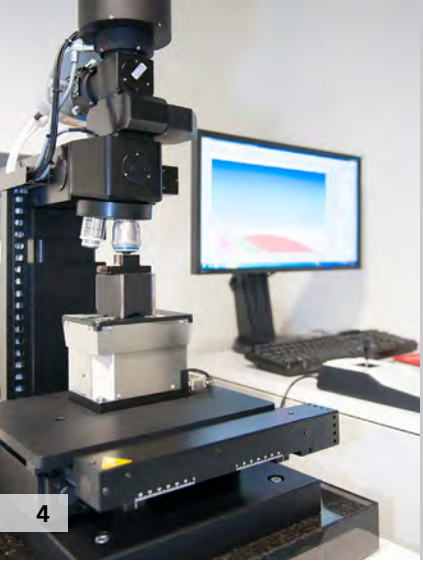
Over the past few years, the Fraunhofer Future Foundation has supported the RIBOLUTION project consortium, which takes an innovative approach to identifying new biomarkers for modern diagnostic solutions. The RIBOLUTION Biomarker Center was set up as part of a close cooperation involving five Fraunhofer institutes and several universities. It was opened on April 26, 2016, at the Fraunhofer Institute for Cell Therapy and Immunology IZI in Leipzig.

At the RIBOLUTION Biomarker Center, novel biomarkers are identified based on ribonucleic acids and developed through to clinical "proof of concept" with the aid of selected patient cohorts. At present, activities are primarily focused on development programs in the areas of prostate cancer, chronic obstructive pulmonary disease (COPD) and infectious diseases.

Biomarker screening and validation

By integrating state-of-the-art genomic analysis methods such as next-generation sequencing (NGS) using our own bioinformatical data analysis methods developed in house, the RIBOLUTION Biomarker Center is able to identify biomarkers and develop new diagnostic tests at the **highest technological level**:

- Illumina HiSeq and Miseq (image 1): Ultra-high-throughput sequencing platforms
- Hamilton Microlab STARlet/STARplus (image 2): Fully automated preparation of samples for sequencing and fully automated extraction and purification of nucleic acids
- Agilent microarray scanner (image 3)
- EMD (image 4): Quality and quantity analyses of minimal amounts of nucleic acids with high sensitivity; developed by Fraunhofer FIT
- QIAcube (image 5): Semi-automated extraction and purification of nucleic acids
- RiBOT (image 6): Novel procedure for the automated validation of biomarkers in high-throughput based on complex interactions between actuator engineering and media to be dispensed; developed by Fraunhofer IPA



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The highest quality standards are defined and implemented from start to finish, which increases the intrinsic value of the obtained data and lays the foundations for the implementation of a quality management system pursuant to DIN ISO 13485, which will become necessary as the project progresses.

New biomarkers are identified and validated using bioinformatical methods. This includes designing custom expression microarrays and analyzing expression microarray data. A proprietary data management system has been developed to store and supply all clinical and experimental data and is used to manage the extensive biobank which has emerged in the RIBOLUTION project.

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BIO-NANOTECHNOLOGY APPLICATION LABORATORY (BNAL)

The Bio-Nanotechnology Application Laboratory (BNAL) in Leipzig represents a research infrastructure jointly run by Fraunhofer IZI and Fraunhofer IKTS. With this laboratory, both institutes are opening up new fields of application in biomedicine related to various nanotechnologies.

State-of-the-art equipment allows biological and medical issues to be handled in an interdisciplinary manner. BNAL provides research and development services from fundamental biomedical research by process development up to the development and validation of innovative technologies and system solutions.

Biological and medical expertise at Fraunhofer IZI (e.g. oncology, chronic inflammatory diseases and neuro-degenerative diseases) in combination with established analysis methods for material diagnostics at Fraunhofer IKTS enable the development of new diagnostic and therapeutic technologies and procedures.

Imaging procedures

- Optical coherence tomography (image 1): Uses near-infrared light to depict the internal and surface structures of various materials in high resolution.
- Multi-acousto-scope: The combination of three microscopy techniques paves the way to innovative new examination strategies.

Cell characterization and classification

- Diagnosis and mapping for cell biology studies: Non-intrusive way of delivering high-resolution, geometric information from the inside of test objects.
- Ultrasound broadband spectroscopy system: This procedure has long been used in the medical diagnosis of cell tissues, biological materials and in the analysis of fluid media. It mainly identifies acoustic and mechanical properties of substances.
- High-throughput flow cytometry (image 2): Rapid, multiplex, high-throughput screening of cells and beads in suspension.
- Fluorescence relaxation for characterizing cells in flow cytometry as a new, label-free procedure that will also be used to characterize cell therapeutic agents and which will be tested on a BD Influx high-throughput cell sorter (image 3).

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Surface sterilization and modification

- Electron beam dosimeter (image 4): Dose measurement of highenergy radiation (e.g. gamma or electron radiation) on even on the different positions of bent 3D free-form surfaces.
- System for electron irradiation of surfaces: Sterilization of package / surfaces, inactivation of microorganisms for vaccine production or targeted adjustment of material properties by means of electron irradiation.

Nanotechnology

- Droplet digital PCR system: PCR-based, absolute quantification of microbial / viral or eukaryotic DNA / RNA as well as precise detection of low genome copy numbers.
- Zetasizer: Determination of particle and molecule sizes, e.g. for characterizing recombinant proteins, micelles and
- nanoparticles.
- Micro-spotter unit (image 5): Automated dosing of tiny quantities of liquid (e.g. biological or organic solutions, or solutions containing nanoparticles) on a broad range of different surfaces for the production of microarrays.
- Hot-embossing system (image 6): Production-relevant manufacturing of nanostructured surfaces on glass and polymer surfaces.

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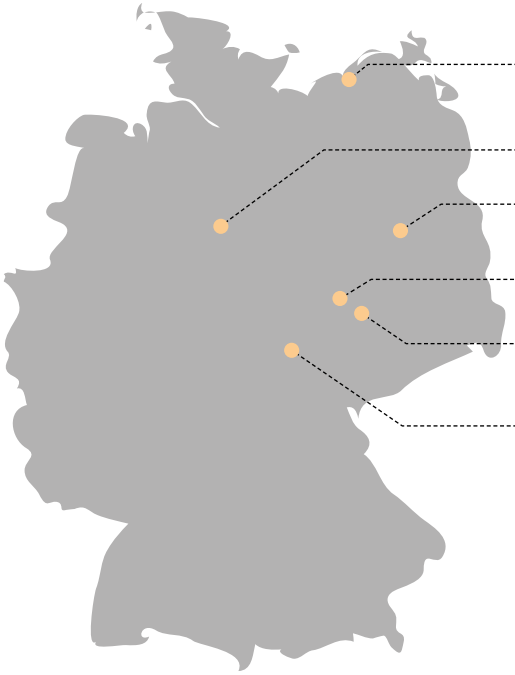
LOCATIONS

THE FRAUNHOFER IZI IN GERMANY AND AROUND THE WORLD



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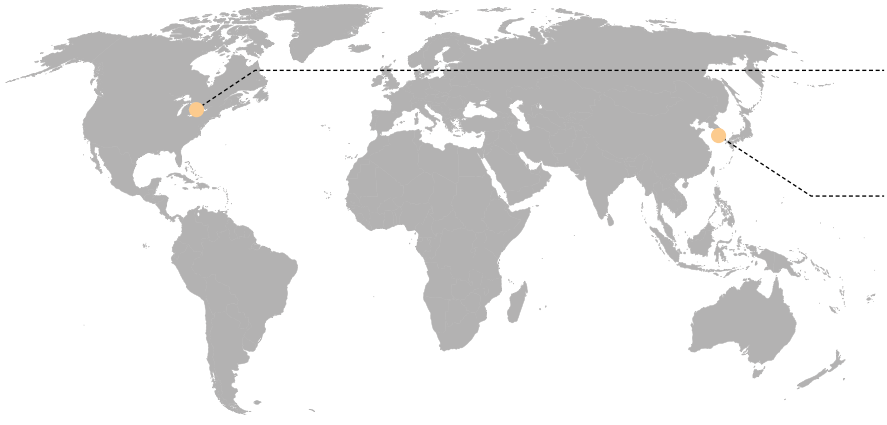
GERMANY

WORLDWIDE



Fraunhofer Project Center for Biomedical Engineering and Advanced Manufacturing (BEAM) at McMaster University, Hamilton, Ontario, Canada

JLCI – Joint Laboratory of Chonnam National University Hospital Hwasun in collaboration with Fraunhofer IZI in Gwangju, Jeollanam-do, South Korea

LEIPZIG HEADQUARTERS, SAXONY, GERMANY

Usable area: 8 749 m²
Employees: 428
Focal areas: Cell engineering, cell therapy, drugs, diagnostics, immunology

Completed in April 2008, the main building boasts extensive laboratory capacities for conducting molecular and cell-biological work. An extensive immunohistochemistry laboratory, an isotope laboratory, a quality control laboratory with qualified equipment, as well as cyro-storage capacities also make up the institute's facilities.

The research infrastructure at the headquarters is complemented by various special facilities found in the extension buildings, which were opened in 2013 and 2015 (e.g. imaging units, laboratories for experimental medicine, a S3 laboratory, and clean-room facilities).

All of the Fraunhofer IZI's laboratories are certified according to S2 standards and therefore suitable for carrying out work in the fields of genetic engineering and infection biology. A flexible cluster structure allows laboratory sections to be adapted and fitted out in line with the specific requirements of a broad range of projects.

The business units Cell and Gene Therapy, Drugs and Diagnostics are primarily based in Leipzig. Biopharmaceutical products for clinical trials are manufactured in line with Good Manufacturing Practice (GMP) in the institute's clean-room facilities, which cover a total area of 1 000 m².

Management

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BIOANALYTICS AND BIOPROCESSING BRANCH OF INSTITUTE IN POTSDAM-GOLM, BRANDENBURG, GERMANY

Usable area: 4 096 m²
Employees: 121
Focal areas: Biotechnology, bioproduction, bioanalytics, automation

The Bioanalytics and Bioprocesses Branch in Potsdam-Golm was affiliated with the Fraunhofer Institute for Cell Therapy and Immunology on July 1, 2014. The site was initially founded in 2005 as a branch of the Fraunhofer IBMT and has since worked on technological solutions for biomedicine and diagnostics as well as for biotechnology and bioproduction.

The interdisciplinary team comprising natural scientists, engineers and technicians develops powerful, analytical methods for the detection and validation of pathogens and biological markers besides processes to obtain, handle and manipulate cells and biomolecules. In this context, the team develops applications for personalized medicine, as well as biosensors and detection procedures for the areas of agriculture and the environment, for a broad spectrum of substance classes.

The site has the state-of-the-art infrastructure required for miniaturizing and automating biological processes. This includes various biosensor and biochip technologies, pipetting robots and micro and nano-dispensers, besides many different rapid-prototyping procedures.

A further special feature of the branch's facilities is the life culture collection of cryophilic algae (CCCryo), which serves as a resource for developing production processes for novel, industrial bioproducts.

Management

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DEPARTMENT OF DRUG DESIGN AND TARGET VALIDATION IN HALLE (SAALE), SAXONY-ANHALT, GERMANY

Usable area: 1 300 m²
Employees: 62
Focal areas: Biochemistry, pharmacology, drug development, analytics

The Department of Drug Design and Target Validation develops new molecular therapies for neurodegenerative and inflammatory diseases. The department's expertise is based on an in depth pharma-like understanding of scientific work and a long-lasting experience in the field of drug development.

This profile encompasses the identification of new target proteins by analyzing putative pathologic post-translational modifications, the misfolding of proteins and the formation of pathological aggregates. Based on these new strategies the department develops and tests small molecules as well as biological agents (biologicals). This research is complemented by the design of new assays for the identification and diagnostic application of biomarkers aiming at monitoring the course of the disease and its therapy.

The department's expertise also expands to the generation of pharmacologically relevant in vitro and in vivo models. Besides state-of-the-art methods for peptide synthesis and protein analytics (MALDI-TOF and LC-MS), the department commands a wide range of biophysical methods to characterize therapeutically relevant physiological pathways, their key proteins as well as cell-based and pharmacologic models for the characterization of new chemical and biological drug candidates.

Management

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DEPARTMENT OF EXTRACORPOREAL IMMUNOMODULATION IN ROSTOCK, MECKLENBURG-WESTERN POMERANIA, GERMANY

Usable area: 700 m²
Employees: 27
Focal areas: Organ-supporting technologies, clinical trials

The department focuses on the development and evaluation of extracorporeal (outside the body) organ-supporting technologies with a particular emphasis on supporting the immune system.

The department offers the full range of preclinical and clinical analyses of extracorporeal technologies on the basis of a broad spectrum of in vitro simulations, small and large animal models as well as a powerful clinical study network for in- and outpatients. Moreover, the group offers self-developed unique analytic and diagnostic devices including an ex situ intestine model, a cell sensor and novel protein assays.

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BRANCH LAB TRANSLATIONAL CELL THERAPY IN HANNOVER, LOWER SAXONY

The Branch Lab Translational Cell Therapy develops and validates cell-based advanced therapy medicinal products (ATMPs). To do this, it conducts translational research and develops GMP-compliant manufacturing protocols for cell therapeutics at the interface to preclinical development right through to their transfer into clinical trials. Cell and genetic engineering methods and strategies are implemented and optimized here to specifically manufacture killer lymphocytes and their subpopulations. The ability to overcome so-called tumor immune escape mechanisms in cancer cells is key here. This is achieved by using activated and genetically modified effector cells together with checkpoint inhibitors and stimulating immune cells. These cell therapies boost immune surveillance and strengthen the elimination of resistant cancer cells as well as their malignant precursor cells (so-called tumor stem cells). Another focus of development lies in optimizing the transduction capacity of effector cells using chimeric antigen receptors (CARs) in order to increase cytotoxicity to malignant cells. To do this, human effector cells are separated following lymphapheresis by means of GMP-suitable, fully automated, closed-system production, genetically modified as necessary and expanded as part of clinical upscaling. Moreover, the group is developing GMP-compliant manufacturing and expansion protocols in order to proliferate a sufficient number of activated effector cells.

Management

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PROJECT CENTER MICROELECTRONIC AND OPTICAL SYSTEMS FOR BIOMEDICINE IN ERFURT, THURINGIA, GERMANY

The Microelectronic and Optical Systems for Biomedicine project center in Erfurt brings together the core competencies of three Fraunhofer institutes to span the disciplines of biosciences, microelectronics, microsystems technology, optics and photonics. This combined expertise will be used to develop application-ready systems in the areas of medical engineering, analytics, diagnostics, biotechnology, biophotonics, pharma, health care, ageing and food economics which will then be transferred into industry. Fields of application here include improved medical imaging and visualization as well as technologies for biomarker analysis.

Involved Fraunhofer Institutes

- Fraunhofer Institute for Applied Optics and Precision Engineering IOF (www.iof.fraunhofer.de/en)
- Fraunhofer Institute for Photonic Microsystems IPMS (www.ipms.fraunhofer.de/en)
- Fraunhofer Institute for Cell Therapy and Immunology IZI (www.izi.fraunhofer.de/en)

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FRAUNHOFER PROJECT CENTER FOR BIO-MEDICAL ENGINEERING AND ADVANCED MANUFACTURING (BEAM) AT MCMASTER UNIVERSITY, HAMILTON, ONTARIO, CANADA

The founding team at Fraunhofer IZI started looking for suitable Canadian cooperation partners back in 2011, a search that led to initial joint research projects being set up with McMaster University in Hamilton (Ontario, Canada). With approximately 29 000 students, the university is one of the most renowned in Canada, with particular strengths in the fields of health sciences, engineering and natural sciences. Over the past four years, McMaster University has attracted the most industry projects of all the universities in Canada.

In 2014, based on the huge success of ongoing cooperation projects, Fraunhofer-Gesellschaft decided to set up a Fraunhofer Project Center (FPC) at McMaster University. Governed by a cooperation agreement, the FPC is jointly run by experienced McMaster and Fraunhofer managers and is devoted to applied research in the business units Diagnostics, Automation, Cell Therapeutics and Biomaterials. Materials researcher Professor John Brennan and expert for bioengineering and drug delivery systems Professor Heather Sheardown are the center's key partners in terms of scientific cooperation and management on the Canadian side of the cooperation. The FPC also helps to establish German and Canadian companies and supports the development of business activities in the respective partner country.

Within the first few months of being established, the project center was already managing to attract significant funding on both the German and Canadian sides, besides a series of industry cooperation projects including approx. 12 million Canadian dollars in FedDev funding awarded in December 2015 for the construction of a joint research building in McMaster Innovation Park, which was opened in spring 2018. The new research building offers a state-of-the-art research infrastructure covering an area of approx. 1 900 m².

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JLCI – JOINT LABORATORY OF CHONNAM NATIONAL UNIVERSITY HOSPITAL HWASUN IN COLLABORATION WITH FRAUNHOFER IZI IN GWANGJU, JEOLLANAM-DO, SOUTH KOREA

Since 2010, Fraunhofer IZI has maintained a close cooperation with Chonnam National University Hospital Hwasun (CNUHH) in several areas. With 700 beds, the CNUHH is one of the largest university hospitals specialized in the treatment of cancer in South Korea. A vibrant biotech and medtech industry has established itself in the local area.

The JLCI facilitates the collaboration with external partners from academia and industry in Asia. For example the Fraunhofer IZI's ligand development group is using the regular access to fresh tumor materials from patients to identify tumor binding peptides, which already have been validated in tumor models.

The laboratory management is oriented at the standards and rules of the Fraunhofer-Gesellschaft. This shall guarantee a common basis when dealing with patents and contractual matters.

The JLCI was financed until 2017 by the Korean Ministry of Education, Science and Technology in Gwangju, Jeollanam-do, South Korea, as part of an initiative to strengthen international cooperation. Since 2018, additional funds have been authorized by the provincial government of Jeollanam do and the district of Hwasun gun in order to facilitate stronger connections within the industry and with other research institutes in Korea and Germany through professional business development.

Various projects have been conducted to date at the JLCI, e.g. in the field of senescence and cancer research, also as part of funding measures associated with the Federal Ministry of Economics and Technology's Central Innovation Program for SMEs. Several Fraunhofer IZI delegations have already taken part in conferences and research stays in Korea and a number of Korean colleagues have also worked at Fraunhofer IZI. The joint research work is documented in many joint publications. German-Korean symposia have so far taken place on an annually rotating basis.

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SCIENCE LOCATION LEIPZIG

LEIPZIG AND THE FORMER TRADE FAIR GROUNDS

The Fraunhofer Institute for Cell Therapy and Immunology IZI is located on the former trade fair grounds in the south-east of the city of Leipzig. Close cooperation with the nearby facilities of the Leipzig University and the companies of the BIO CITY Leipzig is maintained.

Location: Central for interface partners

The Fraunhofer Institute for Cell Therapy and Immunology IZI is located on the former trade fair grounds in the south-east of the city of Leipzig. The institute's premises are only about a ten-minute drive away from the city center and can easily be reached with public transport. Moreover, many of the already established and potential future cooperation partners are located in the immediate vicinity. Among these are, for example, the BIO CITY Leipzig, the Max Planck Institute for Evolutionary Anthropology, the clinics and institutes of the Medical Faculty, the Chemistry Faculty, the Physics Faculty, the Veterinary Medicine Faculty, as well as the Faculty of Life Sciences, Pharmacy and Psychology.

BIO CITY Leipzig: A potent neighbor

The BIO CITY Leipzig unites university and industry-related research under one roof. It houses, for instance, the Biotechnological-Biomedical Center (BBZ) of the Leipzig University and has available space for industrial settlements in the vicinity. More than 25 cell technology companies including VITA34 International AG, Haemabank AG and Curacyte AG are already located there. Cooperations with the Fraunhofer IZI have been established in the fields of cell engineering and applied stem cell biology, bioprocess engineering, protein structure analysis, mass spectroscopy, molecular cell therapy and molecular pathogenesis.

Integrated universities

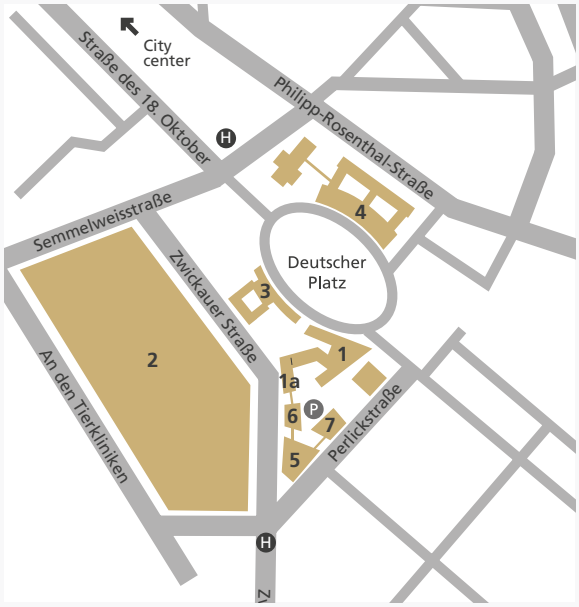
The academic landscape within Leipzig also benefits from cooperation with the Fraunhofer IZI: The Leipzig University, the Leipzig University of Applied Science (HWTK Leipzig) and the Graduate School of Management (HHL) have found in the Fraunhofer IZI a strong partner for research cooperations and the development of joint programs for teaching and advanced vocational training, which enhance local attractiveness from an economic and scientific point of view. Thus, for example, students of business administration from the HHL have already been successfully involved in practical scientific projects with their development of business plans or marketing concepts. A particularly intensive cooperation connects the Fraunhofer IZI and the Institute for Clinical Immunology of the University Leipzig.

The outstanding collaboration work with the Faculty of Veterinary Medicine and its institutes and clinics directly opposite the Fraunhofer IZI building deserves special mention. Research involving animal experiments does not only serve the development of new products for human medicine, but also contributes to the development of new diagnostic and therapeutic procedures in veterinary medicine.

The Faculty of Medicine has traditionally been an extremely important partner with many interactions, also in teaching and advanced education. The Fraunhofer IZI has been working closely together with institutional and clinical areas of radiology, nuclear medicine and diagnostics for several years now in order to develop sophisticated imaging procedures for large animal models.

Numerous partners in the immediate vicinity

The neighboring partners of the Leipzig University are, among others, the Medical Faculty, the Veterinary Medicine Faculty, and the University Hospital. Further institutions relevant for cooperation are the Heart Center Leipzig GmbH, the Helmholtz Center for Environmental Research (UFZ), the Leibniz Institute for Surface Modification (IOM), the Interdisciplinary Center for Bioinformatics (IZBI), the Center for Clinical Trials Leipzig GmbH (ZKS), the Institute for Clinical Immunology, the Center for Biotechnology and Biomedicine (BBZ), and the Max Planck Institute for Human Cognitive and Brain Sciences. Moreover, there are numerous interfaces with different special research areas that are located in Leipzig.



BIO CITY (1) with hired Fraunhofer IZI area (1a), Faculty of Veterinary Medicine, institutes and hospitals (2), Max Planck Institute for Evolutionary Anthropology (3), German National Library (4), Fraunhofer IZI (5), first extension building Fraunhofer IZI (6), second extension building Fraunhofer IZI (7).

EVENTS

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THE FRAUNHOFER IZI IN PUBLIC

Events are the key ingredient of the institute's communication strategy. The Fraunhofer IZI once again organized and supported various scientific and public events in 2018.

New Year's Reception 2018

On January 17, 2018, the Fraunhofer Center for International Management and Knowledge Economy IMW and Fraunhofer IZI held the traditional New Year's reception together. Employees chatted to guests from science, business, politics and culture at the Fraunhofer IMW's headquarters in Leipzig's Städtisches Kaufhaus, where they took stock of the year gone by, discussed new projects, made new contacts and maintained old ones in a celebratory setting. Appointed on December 15, 2017, the new managing director of Fraunhofer IZI, Professor Ulrike Köhl, spoke about her specialist areas in an opening speech. This was followed by an entertaining introductory speech by the founders of digital cultural festival THE ARTS+ and Vice President of Frankfurter Buchmesse Holger Volland, who discussed the question of whether man or machine holds the world's future in their hands. On January 24, 2019, the New Year's reception will be held again at Fraunhofer IZI.

BEAM research building opened

At the McMaster University in Hamilton, Canada, the research building now home to Fraunhofer's BEAM (Biomedical Engineering and Advanced Manufacturing) project center celebrated its opening on March 7, 2018. The project center was set up by Fraunhofer IZI and McMaster University in September 2014 in order to strengthen the research and development capacities of both institutes in the field of applied research. This primarily looks at developments in the areas of regenerative medicine, cell-based therapeutic agents, diagnostic procedures and technologies for the automated manufacture of biomedical products. The new research building in the McMaster Innovation Park, located almost two kilometers from the university campus, offers a state-of-the-art research infrastructure covering an area of approx. 1 900 m². A total of almost 33 million Canadian dollars were invested in the construction project.

1 *Leipzig Fraunhofer institutes' joint New Year's reception.*
2 *Fraunhofer project center BEAM research building opened.*

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Girls'Day 2018 at the Fraunhofer IZI

Girls'Day was held all across Germany on April 26, 2018. Fraunhofer IZI once again took part in the initiative and gave 16 girls from middle and upper school an insight into the work carried out at a biomedical research institute. The pupils were given information on equality, career opportunities and areas of research at Fraunhofer IZI. After listening to a talk on gene therapy entitled "What can we do, what do we want to do, what are we allowed to do?" the girls also had the opportunity to find out more about working in a lab from female researchers from the OpTcell Unit. Among other things, they analyzed cancer cells and stained healthy and diseased tissue under the microscope.

Day of Science Potsdam

For the Day of Science Potsdam held on May 5, 2018, Fraunhofer IZI-BB presented a number of exhibits reflecting the range of research activities at the institute. This included an enlarged 3D model of a rotating mammalian cell, which was suspended contact-free by electric fields in a microfluidic channel. This is used, for instance, to investigate pathological changes in cells taken from a patient's blood without having to touch or mark them. Besides this, the more practical, hands-on experiments also proved to be a hit. Children and adults alike put their experimentation skills to the test and extracted tomato DNA 50 times, built 50 algae reactors and prepared over 100 pH test strips.

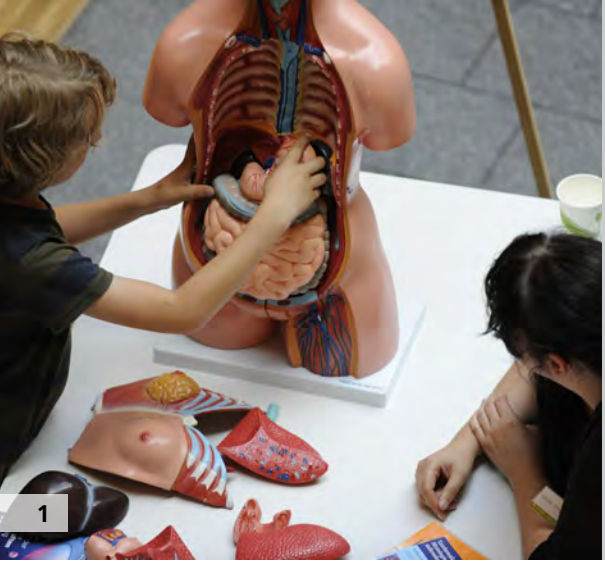
Workshop to improve the treatment of infectious cardiovascular diseases

On the invitation of Professor Andreas Oberbach from Fraunhofer IZI and Professor Christian Hagl, Head of the Cardiac Surgery Clinic at Ludwig Maximilian University of Munich (LMU), international researchers and physicians came together at Fraunhofer IZI on May 15, 2018, to discuss new ways of treating infectious diseases that affect the cardiovascular system. The discussions focused in particular on adsorber systems, which wash out gram-negative bacteria using lipopolysaccharide (LPS) adsorbers in the blood. The event was very much focused on the collaboration between clinical partners, fundamental scientific aspects and industrial feasibility.

1 *Girls'Day 2018 at Fraunhofer IZI.*

2 *Fraunhofer IZI-BB presented the algae reactor for the living room at the Day of Science Potsdam.*

3 *Workshop to improve the treatment of infectious cardiovascular diseases.*



Night of the Sciences in Leipzig: "Uncovering hidden worlds"

Under the motto "Uncovering hidden worlds", Fraunhofer IZI opened its doors to curious guests for Leipzig's Long Night of the Sciences on June 22, 2018. Around 900 visitors stopped by and took the opportunity to microscope cancer cells and learn about the special role stem cells play in the emergence and healing of diseases, or find out how animal experiments are used in new drug development. As in previous years, the tours along the institute's clean rooms proved extremely popular.

Night of the Sciences in Halle (Saale): Drug discovery through computer chemistry and in animal testing

For the Long Night of the Sciences in Halle (Saale) on July 6, 2018, visitors to Fraunhofer IZI were able to discover how modern drug discovery and drug design works using computer chemistry, taking Ibuprofen as an example. Moreover, a number of animal experiments involved in drug discovery for neurodegenerative diseases, especially Alzheimer's disease, were presented in a talk entitled "Animal Ethics and Animal Protection: Animal Testing in Drug Development".

Fraunhofer IZI and Novartis announce continued cooperation at joint press conference

Novartis and Fraunhofer IZI have concluded a further agreement to manufacture CAR-T cell therapies for patients in Europe over the next few years. Launched in 2015, the collaboration to manufacture CAR-T cell therapies for patients taking part in clinical trials initiated by Novartis is therefore being successfully expanded and continued. At a joint press event on August 30, 2018, Novartis, Fraunhofer IZI and investigators from Frankfurt and Cologne university hospitals discussed the mode of action, the manufacturing process and their experiences from the clinical trials so far. Fraunhofer IZI is a key manufacturing and development site for the cell therapy Kymriah® (CTL019), which is provided to patients in Europe taking part in respective clinical trials and compassionate use programs.

1 *Long Night of the Sciences in Leipzig.*

2 *Dr. Gerno Schmiedeknecht (l.) announced the continued cooperation between Novartis and Fraunhofer IZI at the press event.*

Fraunhofer Life Science Symposium in honor of Professor Frank Emmrich

The Fraunhofer Life Science Symposium was held on September 27, 2018, in honor of institute founder Professor Frank Emmrich. Professor Emmrich set up the Fraunhofer Institute for Cell Therapy and Immunology IZI in Leipzig back in 2005. In December 2017, after 13 years of success and strong growth, he handed over the reins to Professor Ulrike Köhl. The 150 invited guests, companions, longstanding research partners, colleagues and members of staff came together with various speakers to look back at key milestones in the career of the renowned immunologist. The president of the Fraunhofer-Gesellschaft Professor Reimund Neugebauer also expressed his thanks.

New Fraunhofer project center "Microelectronic and Optical Systems for Biomedicine" in Erfurt opens its doors

On October 19, 2018, the Fraunhofer project center "Microelectronic and Optical Systems for Biomedicine" (MEOS) celebrated its opening in Erfurt, Thuringia, together with top representatives from the fields of politics, science and business. Three Fraunhofer institutes – the Fraunhofer Institute for Photonic Microsystems IPMS, the Fraunhofer Institute for Applied Optics and Precision Engineering IOF and the Fraunhofer IZI – will conduct joint research projects into new biomedical applications in this area in future, working closely together with business partners.

Annual Conference BioTechnology 2020+

Once a year, the various players from the BioTechnology 2020+ initiative come together for the annual conference. The host this time around was the Fraunhofer-Gesellschaft, more specifically Fraunhofer IZI-BB, which organized the conference at Fraunhofer-Forum Berlin on October 4, 2018. The event was held under the motto "Biological Transformation: Cutting-Edge Technologies in Biomanufacturing", with special attention given to the interface between biology and engineering. The initiative "Next generation of biotechnological procedures – BioTechnology 2020+" was launched by the German Federal Ministry of Education and Research (BMBF) in 2010, together with the major research organizations and the universities. The Fraunhofer-Gesellschaft, the Helmholtz Association, the Leibniz Association and the Max Planck Society have taken it in turns to organize the annual conference since 2014.

1 *Professor Reimund Neugebauer (l.), President of the Fraunhofer-Gesellschaft, expressed his thanks at the Fraunhofer Life Science Symposium in honor of Professor Frank Emmrich.*
2 *Podium discussion at the annual BioTechnology 2020+ conference featuring (f.l.t.r.) Professor Michael Bott, Professor Christine Lang, Dr. Seraphine Wegner, Professor Frank Bier, and host Julia Vismann.*
3 *Insight into the future laboratory spaces of Fraunhofer's MEOS project center.*

LOOKING TO 2019

January 24, 2019
New Year`s Reception

March 28, 2019
Girls'Day 2019 and Boys'Day 2019
www.girls-day.de
www.boys-day.de

April 9, 2019
Science cinema: Film and discussion on cancer medicine

May 11, 2019
Potsdam Day of Science
www.potsdamertagderwissenschaften.de

September 16–17, 2019
Fraunhofer Life Science Symposium & DG-GT Theme Day
www.fs-leipzig.com

SCIENTIFIC PRESENCE

CONVENTIONS AND CONFERENCES

10th Annual PEGS Europe - Protein & Antibody Engineering Summit, November 12–16, 2018, Lisbon, Portugal

10th Autumn School – Current Concepts In Immunology, October 7–12, 2018, Merseburg, Germany

11. Stollberger Onkologiesymposium, November 24, 2018, Oelsnitz / Erzgebirge, Germany

11th Berlin Conference on Life Sciences, March 1–2, 2018, Berlin, Germany

11th FENS Forum of Neuroscience, July 7–11, 2018, Berlin, Germany

14. Nationale Branchenkonferenz Gesundheitswirtschaft 2018, May 24–25, 2018, Warnemünde, Germany

18. biosaxony vor Ort - Stoffwechselerkrankungen und Biopharmazeutika, November 26, 2018, Dresden, Germany

2018 German Biotech Days, April 18–19, 2018, Berlin, Germany

21st Heart of Europe Bio-Crystallography Meeting, September 20–22, 2018, Quedlinburg, Germany

24. GMP Konferenz, December 4–5, 2018, Leipzig, Germany

255th ACS National Meeting (Amercian Chemical Society), March 18–22, 2018, New Orleans, USA

2nd International Symposium on "Allergy meets Infection", September 26–28, 2018, Lübeck, Germany

2nd switchSENSE® User Meeting (Dynamic Biosensors), June 6–8, 2018, Munich, Germany

35th Winter School on Proteinases and Inhibitors, February 28 – March 4, 2018, Tiers am Rosengarten, Italy

4. Interdisziplinäres Schwerpunktsymposium Onkologie (ISSO), January 13, 2018, Lichtenwalde, Germany

56. Wissenschaftliche Tagung der Gesellschaft für Versuchstierkunde GV-Solas, September 12–14, 2018, Munich, Germany

5th Congress of the European Association of Veterinary Laboratory Diagnosticians, October 14–17, 2018, Brussels, Belgium

9th "Physics of Cancer" Symposium, September 24–26, 2018, Leipzig, Germany

Annual Meeting GSEV 2018, March 7–8, 2018, Frankfurt, Germany

BIO 2018, June 4–7, 2018, Boston, USA

Bio Europe® 2018, November 5–7, 2018, Copenhagen, Denmark

Bio Japan 2018, October 10–12, 2018, Yokohama, Japan

BioAsia 2018, February 18–23, 2018, Hyderabad, India

bionection 2018, October 24–25, 2018, Dresden, Germany

Bionnale 2018, June 20, 2018, Berlin, Germany

BIOSAXONY MEETS POLITICS, April 24, 2018, Dresden, Germany

Breath Summit 2018, June 17–20, 2018, Maastricht, The Netherlands

Cell and Gene Meeting on the Mesa, October 3–5, 2018, La Jolla, USA

Concept Heidelberg 10. Single Use Konferenz, December 4–5, 2018, Heidelberg, Germany

Deutsche Innovationspartnerschaft Agrar, March 14, 2018, Bonn, Germany

DNA Nanotechnology 2018, May 24–26, 2018, Jena, Germany

DNA-Mitteldeutschland Spring Meeting 2018, May 24, 2018, Jena, Germany

DNA-Mitteldeutschland Winter Meeting 2018, November 16, 2018, Potsdam, Germany

ECA - GMP for advanced Therapy Medicinal Products, June 21–22, 2018, Berlin, Germany

EIT Health Netzwerktreffen, March 14, 2018, Berlin, Germany

EIT Health Workshop, January 14–16, 2018, Grenoble, France

EIT Health Workshop, November 18–21, 2018, Madrid, Spain

EIT Health Workshop, February 25–28, 2018, Naples, Italy

European Antibody Congress 2018, October 29–31, 2018, Basel, Schwitzerland

European Mass Spectrometry Conference (EMSC) 2018, March 11–15, 2018, Saarbrücken, Germany

FAAM 2018, October 18–21, 2018, Copenhagen, Denmark

Forum Veterinärdiagnostik, January 23, 2018, Berlin, Germany

Fraunhofer Life Science Symposium 2018, September 27, 2018, Leipzig, Germany

Fraunhofer-Symposium "Netzwert" 2018, February 27–28, 2018, Munich, Germany

FUTURAS IN RES - Biological Transformation, June 28–29, 2018, Berlin, Germany

GvH/GvL 2018, 14th International Symposium, March 7–9, 2018, Regensburg, Germany

Hacking Female Health Hackathon, November 2–4, 2018, Berlin, Germany

Hämatologisch-onkologisches Symposium, April 21, 2018, Lichtenwalde, Germany

ICCAS-Statusseminar, January 18, 2018, Leipzig, Germany

in-cosmetics global 2018, April 17–19, 2018, Amsterdam, The Netherlands

Infections'21 Symposium: Interdisciplinary Approaches to Infectious Disease Research, June 14, 2018, Leipzig, Germany

InnoCON Thüringen 2018, November 27, 2018, Erfurt, Germany

INNO-Convention 2018 - Landwirtschaft gestaltet Zukunft (mit), May 31, 2018, Dresden, Germany

InnoHealth Australia InnovationPlatform, April 10–11, 2018, Melbourne, Australia

International Conference on Traditional Medicine, Phytochemistry and Medicinal Plants (TMedPM-2018), October 15–17, 2018, Chiba, Japan

ISCT 2018, May 1–5, 2018, Montreal, Canada

Keystone Symposia Exosomes / Microvesicles, June 4–8, 2018, Breckenridge, USA

LOUNGES 2018, February 6–8, 2018, Karlsruhe, Germany

MEDICA 2018, November 12–15, 2018, Düsseldorf, Germany

Pharma Congress Production & Technology 2018, April 23–25, 2018, Düsseldorf, Germany

PolyMerTec18, June 13–15, 2018, Merseburg, Germany

Sachsen global vernetzt (WFS), April 10, 2018, Dresden, Germany

Sartorius Research Xchange Forum 2018, March 20–21, 2018, Göttingen, Germany

Soft Matter Day 2018, July 6, 2018, Leipzig, Germany

The Product is the Process - Is it? Qualitätsaspekte bei der Herstellung von ATMP, November 13, 2018, Potsdam, Germany

Tumor Immunology meets Oncology XIV, May 24–26, 2018, Halle (Saale), Germany

World Advanced Therapies & Regenerative Medicine 2018, May 15–20, 2018, London, Great Britain

XPomet© Convention 2018, March 21–23, 2018, Leipzig, Germany

RESEARCH PARTNERS

AIT Austrian Institute of Technology, Vienna, Austria

Anhalt University of Applied Sciences, Köthen, Germany

Aristotle University of Thessaloniki, Thessaloniki, Greece

Asociación de la Industria Navarra, Cordovilla, Spain

Babraham Institute, Cambridge, Great Britain

Berlin-Brandenburg Center for Regenerative Therapies BCRT, Berlin, Germany

Beuth University of Applied Sciences Berlin, Berlin, Germany

Bielefeld University, Bielefeld, Germany

Biomedical Primate Research Centre, Rijkswijk, The Netherlands

Brandenburg University of Technology Cottbus-Senftenberg, Senftenberg, Germany

Brigham & Women's Hospital, Harvard Medical School, Boston, USA

Bundesanstalt für Materialforschung und -prüfung (BAM), Berlin, Germany

Caritas Hospital St. Josef, University of Regensburg, Regensburg, Germany

Centro Tecnológico L'Urederra, Navarra, Spain

Charité - Universitätsmedizin Berlin, Berlin, Germany

Chonnam National University, Hwasun, South Korea

CIDEIM Centro Internacional de Entrenamiento e Investigaciones Medicas, Cali, Colombia

Coburg University of Applied Sciences and Arts, Coburg, Germany

Dhirubhai Ambani Institute of Information and Communication Technology, Gandhinagar, India

Erasmus MC, Rotterdam, The Netherlands

Essen University Hospital, Essen, Germany

Experimental and Clinical Research Center (ECRC), Berlin, Germany

Federal University of Rio de Janeiro, Rio de Janeiro, Brasil

FH Aachen University of Applied Sciences, Jülich, Germany

Flensburg University of Applied Sciences, Flensburg, Germany

Forschungszentrum Jülich, Jülich, Germany

Fraunhofer Institute for Applied Information Technology FIT, Sankt-Augustin, Germany

Fraunhofer Institute for Applied Polymer Research IAP, Potsdam, Germany

Fraunhofer Institute for Biomedical Engineering IBMT, St. Ingbert, Germany

Fraunhofer Institute for Ceramic Technologies and Systems IKTS, Dresden, Germany

Fraunhofer Institute for Chemical Technology ICT, Pfinztal, Germany

Fraunhofer Institute for Electronic Nano Systems ENAS, Chemnitz, Germany

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

Fraunhofer Institute for Manufacturing Engineering and Automation IPA, Stuttgart, Germany

Fraunhofer Institute for Manufacturing Technology and Advanced Materials IFAM, Bremen, Germany

Fraunhofer Institute for Microstructure of Materials and Systems IMWS, Halle (Saale), Germany

Fraunhofer Institute for Molecular Biology and Applied Ecology IME, Aachen, Germany

Fraunhofer Institute for Organic Electronics, Electron Beam and Plasma Technology FEP, Dresden, Germany

Fraunhofer Institute for Photonic Microsystems IPMS, Dresden, Germany

Fraunhofer Institute for Process Engineering and Packaging IVV, Freising, Germany

Fraunhofer Institute for Reliability and Microintegration IZM, Berlin, Germany

Fraunhofer Institute for Toxicology and Experimental Medicine ITEM, Hannover, Germany

Fraunhofer Research Institution for Marine Biotechnology and Cell Technology EMB, Lübeck, Germany

Freie Universität Berlin, Berlin, Germany

Friedrich Schiller University Jena, Jena, Germany

Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany

Furtwangen University, Villingen-Schwenningen, Germany

German Aerospace Center (DLR), Berlin, Germany

German Cancer Research Center (Deutsches Krebsforschungszentrum DKFZ), Heidelberg, Germany

German Federal Institute for Risk Assessment (BfR), Berlin, Germany

German Institute of Human Nutrition, Potsdam, Germany

German Primate Center, **Leibniz Institute for Primate Research,** Göttingen, Germany

German Rheumatism Research Centre Berlin (DRFZ), Berlin, Germany

Ghent University, Ghent, Belgium

Hannover Medical School (MHH), Hannover, Germany

Harvard Medical School, Boston, USA

Heinrich Heine University Düsseldorf, Düsseldorf, Germany

Helmholtz Centre for Environmental Research UFZ, Leipzig, Germany

Helmholtz Centre for Infection Research, Braunschweig, Germany

Helmholtz Centre Potsdam, **GFZ German Research Centre for Geosciences,** Potsdam, Germany

Hochschule Hannover - University of Applied Sciences and Arts, Hannover, Germany

Hospital Chemnitz, Chemnitz, Germany

Hospital St. Elizabeth and St. Barbara, Halle (Saale), Germany

Hudson Institute of Medical Research, Melbourne, Australia

Humboldt-Universität zu Berlin, Berlin, Germany

Innovations for High Performance Microelectronics, **Leibniz-Institut für innovative Mikroelektronik,** Frankfurt (Oder), Germany

Institut Dr. Schulze GbR, Markkleeberg, Germany

Institut du Cerveau et de la Moelle épinière – ICM (Brain & Spine Institute), Paris, France

Institute for Bioprocessing and Analytical Measurement Techniques (iba), Heilbad Heiligenstadt, Germany

Instituto Politécnico Nacional, Ciudad de México, México

Jagiellonian University, Krakow, Poland

Julius Kühn Institute (JKI) Federal Research Centre for Cultivated Plants, Siebeldingen, Germany

Karolinska Institutet, Stockholm, Sweden

Kiel University (CAU), Kiel, Germany

KU Leuven, Leuven, Belgium

Leibniz Institute for Plasma Science and Technology (INP Greifswald), Greifswald, Germany

Leibniz Institute of Surface Engineering (IOM), Leipzig, Germany

Leibniz Institute of Vegetable and Ornamental Crops (IGZ), Großbeeren, Germany

Leipzig Heart Center , Leipzig, Germany

Leipzig University of Applied Sciences (HTWK Leipzig), Leipzig, Germany

Leipzig University, Leipzig, Germany

Liverpool School of Tropical Medicine, Liverpool, Great Britain

Ludwig-Maximilians-Universität München, Munich, Germany

Makerere University, Kampala, Uganda

Marien Hospital Herne – Universitätsklinikum der Ruhr-Universität Bochum, Herne, Germany

Martin Luther University Halle-Wittenberg, Halle (Saale), Germany

Max Delbrück Center for Molecular Medicine, Berlin, Germany

Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Max Planck Institute of Molecular Plant Physiology, Potsdam, Germany

McGill University, Montreal, Canada

McMaster University and St. Joseph's Healthcare, Hamilton, Canada

McMaster University, Hamilton, Canada

MD Anderson Cancer Center, Houston, USA

Monash University, Melbourne, Australia

Multitel, Mons, Belgium

National Autonomous University of Mexico (UNAM), Ciudad de México, Mexico

National Centre for Scientific Research "Demokritos", Athens, Greece

National Institute for Standards and Technology (NIST), Gaithersburg, USA

Nottingham Trent University, Nottingham, Great Britain

Otto von Guericke University Magdeburg, Magdeburg, Germany

Paul Flechsig Institute of Brain Research, Leipzig, Germany

Pilot Vegetable Oil Technology (PPM), Magdeburg, Germany

Potsdam Institute for Climate Impact Research, Potsdam, Germany

Research Center Borstel, **Leibniz Lung Center,** Borstel, Germany

Robert Koch Institute, Berlin, Germany

Rostock University Medical Center, Rostock, Germany

Ruhr-Universität Bochum, Bochum, Germany

Rural Service Center of Rhineland-Palatinate, Bernkastel, Germany

Saarland University, Homburg, Germany

Saxony State Office for the Environment, Agriculture and Geology, Köllitsch, Germany

Seoul National University, Seoul, South Korea

Technical University of Applied Sciences Wildau, Wildau, Germany

Technical University of Munich, Munich, Germany

Technische Universität Berlin, Berlin, Germany

Technische Universität Braunschweig, Braunschweig, Germany

Technische Universität Dresden, Dresden, Germany

Tel Aviv University, Tel Aviv, Israel

Thüringer Tierseuchenkasse, Jena, Germany

Ulm University, Ulm, Germany

Universität Braunschweig, Braunschweig, Germany

University Hospital Dresden, Dresden, Germany

University Hospital Erlangen, Erlangen, Germany

University Hospital Halle (Saale), Halle (Saale), Germany

University Hospital of the Saarland, Homburg, Germany

University Hospital of Würzburg, Würzburg, Germany

University Hospital Regensburg, Regensburg, Germany

University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany

University Medical Center Mainz, Mainz, Germany

University Medical Center Schleswig-Holstein (UKSH), Kiel, Germany

University of Applied Sciences Bremerhaven, Bremerhaven, Germany

University of Applied Sciences Jena, Jena, Germany

University of Belgrade, Belgrade, Serbia

University of Bergen, Bergen, Norway

University of Bern, Bern, Schwitzerland

University of Bonn, Bonn, Germany

University of California, San Diego, USA

University of Cambridge, Cambridge, Great Britain

University of Cologne, Cologne, Germany

University of Freiburg, Freiburg, Germany

University of Göttingen, Göttingen, Germany

University of Graz, Graz, Austria

University of Greifswald, Greifswald, Germany

University of Innsbruck, Innsbruck, Austria

University of Kassel, Kassel, Germany

University of Leipzig Medical Center, Leipzig, Germany

University of Oslo, Oslo, Norway

University of Oxford, Oxford, Great Britain

University of Padova, Padova, Italy

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University of Zurich, Zurich, Schwitzerland

UP Transfer GmbH, Potsdam, Germany

Uppsala University, Uppsala, Schweden

Washington University School of Medicine, St. Louis, USA

2bind GmbH, Regensburg, Germany

3B Pharmaceuticals, Berlin, Germany

Affimed GmbH, Heidelberg, Germany

Airbus AG, Hamburg, Germany

AJ Innuscreen GmbH, Berlin, Germany

AJ Roboscreen GmbH, Leipzig, Germany

AKT Angewandte Kommunikationstechnik GmbH, Beucha, Germany

Albutec GmbH, Rostock, Germany

Analytik Jena AG, Jena, Germany

Anapath Services GmbH, Liestal, Switzerland

AptaIT GmbH, Munich, Germany

Artcline GmbH, Rostock, Germany

ASA Spezialenzyme GmbH, Wolfenbüttel, Germany

Asahi Kasei, Tokyo, Japan

Baxter Deutschland GmbH, Unterschleißheim, Germany

Becit GmbH, Bitterfeld-Wolfen, Germany

Befort Wetzlar OD GmbH, Wetzlar, Germany

BellaSeno GmbH, Leipzig, Germany

Berlin Heart GmbH, Berlin, Germany

Berthold Technologies, Bad Wildbad, Germany

Biametrics, Tübingen, Germany

BianoGMP GmbH, Gera, Germany

Bianoscience GmbH, Gera, Germany

Bill and Melinda Gates Foundation, Seattle, USA

BioArtProducts GmbH, Rostock, Germany

BioGenes GmbH, Berlin, Germany

BIOSYNTAN GmbH, Berlin, Germany

biotechrabbit GmbH, Henningsdorf, Germany

BioTeZ Berlin Buch GmbH, Berlin, Germany

Boehringer Ingelheim Animal Health, Hannover, Germany

Boehringer Ingelheim VRC GmbH & Co. KG, Hannover, Germany

Brandenburg Antiinfektiva GmbH, Borstel, Germany

Cellavent GmbH, Düsseldorf, Germany

CellTrend GmbH, Luckenwalde, Germany

Clearum GmbH, Rostock, Germany

C-Lecta GmbH, Leipzig, Germany

CNM Technologies GmbH, Bielefeld, Germany

Cogen Therapeutics, Cambridge, MA, USA

CONGEN Biotechnologie GmbH, Berlin, Germany

CureVac AG, Tübingen, Germany

CytoSorbents Europe GmbH, Berlin, Germany

Daiichi-Sankyo, Tokyo, Japan

DMCE GmbH & Co KG, Linz, Austria

DOKAtec GmbH, Sömmerda, Germany

DYN Labs Ltd., Caesarea, Israel

Enzo Life Sciences (ELS) AG, Lausen, Switzerland

Epiontis GmbH, Berlin, Germany

Epitopic GmbH, Leipzig, Germany

ERT-OPTIK Dr. Thiel GmbH, Ludwigshafen, Germany

Evonik Creavis GmbH, Marl, Germany

Experimental Pharmacology & Oncology Berlin-Buch GmbH, Berlin, Germany

FIM Biotech GmbH, Berlin, Germany

Fresenius Kabi Deutschland GmbH, Bad Homburg, Germany

fzmb GmbH, Bad Langensalza, Germany

Geräte- und Vorrichtungsbau Spitzner OHG, Leipzig, Germany

GeSIM Gesellschaft für Silizium-Mikrosysteme mbH, Radeberg, Germany

Glycotope GmbH, Berlin, Germany

GVG Diagnostics GmbH, Leipzig, Germany

humatrix AG, Pfungstadt, Germany

IBA Lifesciences, Göttingen, Germany

Ichor Medical Systems, Inc., San Diego, USA

Icon Genetics, Halle (Saale), Germany

Idifarma Desarrollo Farmacéutico, S.L., Navarra, Spain

IDT Biologika GmbH, Dessau-Roßlau, Germany

IgNova GmbH, Oberursel, Germany

ILBC GmbH, Potsdam, Germany

Immunic AG, Martinsried, Germany

IMT Masken und Teilungen AG, Greifensee, Switzerland

in.vent DIAGNOSTICA GMBH, Hennigsdorf, Germany

Innovative Molecules GmbH, Bad Salzuflen, Germany

Institut für Produktqualität GmbH, Berlin, Germany

InstrAction GmbH, Mannheim, Germany

InVivo Biotech Services, Berlin, Germany

Ionera Technologies GmbH, Freiburg, Germany

Iovance Biotherapeutics Inc, San Carlos, USA

Ipratech SA, Mons, Belgium

KET Kunststoff- und Elasttechnik GmbH, Radeberg, Germany

Klinik und Poliklinik für Neurochirurgie, Leipzig, Germany

Lipocalyx GmbH, Halle (Saale), Germany

LOHMANN TIERZUCHT GmbH, Cuxhaven, Germany

Lufthansa Technik AG, Hamburg, Germany

M2-Automation, Berlin, Germany

Magna Diagnostics GmbH, Leipzig, Germany

MEDAC, Wedel, Germany

Medichema GmbH, Chemnitz, Germany

Medipan, Dahlewitz, Germany

Mibelle Biochemistry, Mibelle AG, Buchs, Switzerland

MicroDiscovery GmbH, Berlin, Germany

microfluidic ChipShop GmbH, Jena, Germany

Micro-Hybrid Electronic GmbH, Hermsdorf, Germany

Mikrogen, Munich, Germany

Moderna Therapeutics, Cambridge, MA, USA

nal von minden GmbH, Regensburg, Germany

Nanion Technologies GmbH, Munich, Germany

NanoBioAnalytics, Berlin, Germany

Navigo Proteins GmbH, Halle (Saale), Germany

new/era/mabs, Potsdam, Germany

Nipro Europe NV, Brussels, Belgium

Nomad Bioscience GmbH, Halle (Saale), Germany

Northwest Biotherapeutics GmbH, Leipzig, Germany

Novartis Pharma AG, Basel, Switzerland / Morris Plains, USA

Novartis Pharma GmbH, Nuremberg, Germany

NovaTec Immundiagnostica GmbH, Dietzenbach, Germany

Novavax AB, Uppsala, Sweden

NTG Neue Technologien GmbH & Co. KG, Gelnhausen, Germany

opTricon – Entwicklungsgesellschaft für Optische Technologien mbH, Berlin, Germany

PerformaNat GmbH, Berlin, Germany

Piculet Biosciences, Leiden, The Netherlands

Plexense, Inc., Gyeonggi-do, South Korea

PolyAn GmbH, Berlin, Germany

PolyQuant GmbH, Bad Abbach, Germany

Praxis Pharmaceutical, Miñano, Spain

Preclinics, Potsdam, Germany

Primacyt GmbH, Schwerin, Germany

Primedica GmbH, Dortmund, Germany

Probiodrug AG, Halle (Saale), Germany

Qiagen GmbH, Leipzig, Germany

quartett Immunodiagnostika, Biotechnologie + Kosmetik Vertriebs GmbH, Berlin, Germany

Quimatryx S.L., San Sebastian, Spain

Rathenower Optik GmbH, Rathenow, Germany

RedHill Biopharma Ltd., Tel Aviv, Israel

Redivia, Dresden, Germany

ReliaTech Receptor Ligand Technologies GmbH, Wolfenbüttel, Germany

RESprotect GmbH, Dresden, Germany

Roche Glycart AG, Schlieren, Switzerland

Rudolf-Boehm-Institut für Pharmakologie und Toxikologie, Leipzig, Germany

Sartorius Stedim Biotech GmbH, Göttingen, Germany

SB Science Management, Berlin, Germany

Schmuhl-Faserverbundtechnik, Remptendorf, Germany

Scienion AG, Berlin, Germany

Scienova, Jena, Germany

Sciomics, Heidelberg, Germany

Secopta GmbH, Berlin, Germany

SelfDiagnostics Deutschland GmbH, Leipzig, Germany

Seramun Diagnostica GmbH, Heidesee, Germany

Serumwerk Bernburg, Bernburg, Germany

SerYmun Yeast GmbH, Halle (Saale), Germany

SFC Co., Ltd., Yongin-si, South Korea

Siemens AG, Munich / Erlangen, Germany

SKW Stickstoffwerke Piesteritz GmbH, Lutherstadt Wittenberg, Germany

Sonovum, Leipzig, Germany

Surflay Nanotec GmbH, Berlin, Germany

Tcell Tolerance GmbH, Leipzig, Germany

Trifolio-M GmbH, Lahnau, Germany

TWINCORE, Zentrum für Experimentelle und Klinische Infektionsforschung GmbH, Hannover, Germany

Vaccinex, Rochester, NY, USA

Villeroy & Boch, Mettlach, Germany

Vita 34 AG, Geschäftsbereich BioPlanta, Leipzig, Germany

We love apps, Erfurt, Germany

WISAG AG, Frankfurt, Germany

Wrig Nanosystems GmbH, Leipzig, Germany

Yumab GmbH, Braunschweig, Germany

Zellmechanik Dresden GmbH, Dresden, Germany

TEACHING ACTIVITIES

Anhalt University of Applied Sciences

Protein biotechnology (lecture), Prof. Dr. Hans-Ulrich Demuth

Beuth University of Applied Sciences Berlin

Proteomics (training), PD Dr. Harald Seitz

Selected aspects of biotechnology: Cell free protein synthesis (lecture), Dr. Stefan Kubick

Fraunhofer IZI

Education and training of persons carrying out animal experiments (Category B / FELASA) (course), Dr. Thomas Grunwald, Dr. Franziska Lange, Karoline Möller, Dr. Antje Dreyer, Christiane Storch

TECAN Freedom EVO 100 - use and programming (course), Dr. Arndt Wilcke

Free University of Berlin

Cell-free Synthesis of Membrane Proteins (training), Dr. Stefan Kubick

Cell-free Synthesis of Membrane Proteins (seminar), Dr. Stefan Kubick

Membrane Proteins: Classification,Structure and Function (lecture), Dr. Stefan Kubick

Indian Institute of Technology Madras

Smart Molecules (lecture), Dr. David M. Smith

Klinikum Chemnitz gGmbH

Advanced training for Physician Assistants in Internal Medicine (training), PD Dr. Stephan Fricke

Practical training / students Internal Medicine (training), PD Dr. Stephan Fricke

Leipzig University

Animal models in preclinical development (lecture), Dr. Ulla Slanina

Aquatic experimental animals (lecture), Dr. Thomas Grunwald

Autoimmune diseases (seminar), Dr. Thomas Grunwald

Environmental medicine for adults 2 (course), Dr. Jana Burkhardt

Environmental medicine for adults 2 (course), Susanne Przybylski-Wartner

GLP / GMP (lecture), Dr. Jörg Lehmann / Dr. Maximilian Hoffmann

Infection immunology, virology (lecture), Dr. Thomas Grunwald

International regulations for medicinal products, EMA and FDA / strategies and methods for immunotoxicity testing of chemicals and medicinal products (lecture), Dr. Jörg Lehmann

Molecular medicine / virology (lecture), PD Dr. Sebastian Ulbert

Molecular medicine / virology (training), PD Dr. Sebastian Ulbert

Morphology and function of immunological cells and organs / basic functions of the immune system (lecture), Dr. Jörg Lehmann

Organic chemistry (training), Dr. Daniel Ramsbeck

Paramyxoviruses (lecture), Dr. Thomas Grunwald

Pharmaceutical analytics / Drug monitoring II (lecture), Dr. Mirko Buchholz

Pharmaceutical biology / immunology (lecture), Dr. Jörg Lehmann

Preclinical in vitro and in vivo models for the detection and evaluation of immunotoxic effects of medicinal products (lecture), Sina Riemschneider

Preclinical in vitro and in vivo models for the detection and evaluation of immunotoxic effects of medicinal products and chemicals (lecture), Sina Riemschneider

QSB4 Autoimmunity (course), Dr. Peter Ruschpler

QSB4 lecture series "infectiology / immunology" transplantation immunology (lecture), Dr. Anna Kretschmer

QSB6 Environmental medicine for adults 1 (seminar), Lilly Stahl

QSB6 Environmental medicine for adults 2 (seminar), Lilly Stahl

Statistical learning (lecture), Dr. Kristin Reiche, Dr. David Petroff, Dr. Andreas Kühnapfel, Prof. Dr. Martin Bogdan

Supervision of PhD students (seminar), PD Dr. Stephan Fricke

Tumor vaccination (lecture), Dr. Thomas Grunwald

Vector-borne virus infection (lecture), PD Dr. Sebastian Ulbert

Virology (training), Dr. Thomas Grunwald, Nadja Lindner, Leila Issmail

Viruses of the respiratory tract (lecture), Dr. Thomas Grunwald

Leipzig University of Applied Sciences (HTWK Leipzig)

Bioreactors (lecture), Prof. Dr. Ulf-Dietrich Braumann

Biostatistics (lecture), Prof. Dr. Ulf-Dietrich Braumann

Image processing (lecture), Prof. Dr. Ulf-Dietrich Braumann

Laboratory techniques (lecture), M.Sc. Elisabeth Wenzel

Microscopic imaging (lecture), Prof. Dr. Ulf-Dietrich Braumann

Microscopic image processing (lecture), Prof. Dr. Ulf-Dietrich Braumann

Recombinant protein production in a bioreactor using the example of monoclonal antibodies – critical process parameters and control – GMP production (lecture), Dr. Maximilian Hoffmann

Stem cell biology (lecture), Dr. Claire Fabian

Martin Luther University Halle-Wittenberg

Applied cheminformatics for bioinformaticians (lecture), Dr. Mirko Buchholz

Applied cheminformatics for bioinformaticians (seminar), Dr. Mirko Buchholz, Christian Jäger

Applied cheminformatics for bioinformaticians (training), Christian Jäger

extracurricular: Summer School ChemInformatics GdCh, Dr. Mirko Buchholz

Lab Course on Vector Construction (training), Dr. Stephan Schilling

Molecular Biotechnology: Construction of Hosts and Vectors (lecture), Dr. Stephan Schilling

Non-curricular teaching (module supervision in the master program biochemistry) (training), Dr. Holger Cynis

Peter Debye Institute, Leipzig University

Experimental Physics IV – Thermodynamics and Soft Matter Physics (seminar), Paul Mollenkopf

Soft Matter and Biological Physics (seminar), Dr. David M. Smith

Soft Matter and Biological Physics (lecture), Dr. Jörg Schnauß

Technical University of Berlin

Cell free synthesis of membrane proteins (training), Dr. Stefan Kubick

Membrane proteins: Classification, structure and function (lecture), Dr. Stefan Kubick

University of Potsdam

Applied limnology: Snow algae as an interesting bioresource for basic research and industrial bioproduction of algal metabolites (lecture), Dr. Thomas Leya

Biotechnological methods (seminar), PD Dr. Harald Seitz

Cell-free Protein Synthesis, (lecture), Dr. Stefan Kubick

Cell-free Synthesis of Membrane Proteins (seminar), Dr. Stefan Kubick

Cell-free Synthesis of Membrane Proteins (training), Dr. Stefan Kubick

EVALUATOR ACTIVITIES

Alexander von Humboldt-Stiftung, Prof. Dr. Dr. Ulrike Köhl

ACS Materials and Interfaces, Dr. Claus Duschl

Advances in Dairy Research, Dr. Jörg Lehmann

Alzheimer's Association (USA), Dr. Holger Cynis

Alzheimer's Society (UK), Dr. Holger Cynis

Blood Reviews, Prof. Dr. Dr. Ulrike Köhl

BMC Bioinformatics, Michael Rade

Cytometry Part A, Prof. Dr. Attila Tárnok

Deutsche Forschungsgemeinschaft (DFG), Prof. Dr. Dr. Ulrike Köhl, Prof. Dr. Frank Emmrich

European Society for Blood and Marrow Transplantation, Prof. Dr. Dr. Ulrike Köhl

Emerging Micobes and Infections, PD Dr. Sebastian Ulbert

European Research Council, Dr. Holger Cynis

Faculty 1000, Dr. Jörg Lehmann

Frontiers Immunology, Prof. Dr. Dr. Ulrike Köhl

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PUBLICATIONS

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Köhl U. **From CAR T cells to CAR expressing NK cells: Good candidate for off the shelf ATMP?**.Tagung CAR-T-Zellen, January 30–31, 2018, Berlin, Germany

Köhl U. **Verteidigung des Proof-of-Concept-Antrags »iPSC-based Macrophage Therapy Targeting Chronic Respiratory Infections«**. Förderung von Kooperationen zwischen der Helmholtz-Gemeinschaft, der Fraunhofer-Gesellschaft und der Deutschen Hochschulmedizin als Pilotprojekte für eine Proof-of-Concept-Plattform, February 1–2, 2018, Berlin, Germany

Köhl U. **CD20CAR transduced T cells for individualized Melanoma Therapy**. Annual Meeting Clustertreffen CD20 CAR-Time, February 22–23, 2018, Cologne, Germany

Köhl U. **Aktivierte und gerichtete NK-Zellen zur Tumortherapie und zur Toleranzinduktion**. 22. Jahressymposium der IGLD (Interdisziplinäre Gruppe für Labor und Durchflusszytometrie), March 1–3, 2018, Frankfurt/Main, Germany

Köhl U. **From CAR T cells to CAR NK cells: Do we need both?**.IFB-Tx (Integrated Research and Treatment Center Transplantation) Symposium: Perspectives in Transplantation, March 8–9, 2018, Hannover, Germany

Köhl U. **CAR expressing effector cells for cancer treatment**. Frontiers in Medicinal Chemistry 2018, Gesellschaft Deutscher Chemiker e.V. (GDCh), March 11–14, 2018, Jena, Germany

Köhl U. **CAR expressing effector cells in stem cell transplantation**. ICKSH 2018 – 2018 Korean Society of Hematology International Conference & 59th Annual Meeting, March 29–30, 2018, Seoul, South Korea

Köhl U. **Next Generation Immunonkologie: Status quo der zellulären Therapie CAR-T-Zellen bei GI-Tumoren?**. GI-Oncology 2018, June 8–9, 2018, Wiesbaden, Germany

Köhl U. **Hohe Forschungsaufwendungen in der Medizin sind nur in guten Netzwerken zu stemmen**. Parlamentarischer Abend »Medizinische FuE in Niedersachsen«, June 21, 2018, Hannover, Germany

Köhl U. **Diagnostics for individualized infection medicine**. Herrenhausen Symposium »Individualized Infection Medicine - The future is now«, June 21–23, 2018, Hannover, Germany

Köhl U. **CAR expressing effector cells for cancer retargeting**. Klinik für Pädiatrie mit Schwerpunkt Onkologie und Hämatologie der Charité – Universitätsmedizin Berlin, August 27, 2018, Berlin, Germany

Köhl U. **Personalisierte Medizin – Immunonkologie**. Herbstsitzung der Interministeriellen Arbeitsgruppe »Biotechnologie-Offensive Sachsen« der Sächsischen Staatsministerien, September 6, 2018, Dresden, Germany

Köhl U. **Manufacturing of cell-based therapies for Inner ear**. 55th Inner Ear Biology Workshop, September 6–8, 2018, Berlin, Germany

Köhl U. **Automatisierung von CAR-Effektorzellen**. Von BiTES, CAR-T und mehr: Möglichkeiten, Probleme und Grenzen der zellulären Therapie mit T-Zellen. Symposium der Cellex Academy, September 14, 2018, Cologne, Germany

Köhl U. **Automation for CAR effector cells: Improved design of ATMP manufacturing processes**. APV Interactive Workshop on ATMP »Bridging standard pharma concepts and ATMP«, September 27–28, 2018, Vienna, Austria

Köhl U. **CAR expressing effector cells for cancer retargeting**. Tummorimmunologie, October 4, 2018, Vienna, Austria

Köhl U. **Network for cell and gene therapy**. Karolinska Institutet, October 11–13, 2018, Stockholm, Sweden

Köhl U. **CAR NK cells for cancer retargeting**. International Symposium on Cancer-Immuno-Oncology, October 17–18, 2018, Lübeck, Germany

Köhl U. **Immun Escape (Fokus NK-Zelle)**. Immunonkologischer Differenzierungsworkshop, November 2–3, 2018, Frankfurt/Main, Germany

Köhl U. **CAR expressing NK cell-based immunotherapy for cancer retargeting**. 10th Annual PEGS Europe, November 12–16, 2018, Lisbon, Portugal

Köhl U. **Podiumsdiskussion: Zell- & Gentherapeutika – Eine finanzielle Herausforderung für das Gesundheitssystem?**. Hauptstadt Summit House of Pharma & Healthcare, November 20, 2018, Berlin, Germany

Köhl U. **Opening-Vortrag: The Era of Gene Therapy; Podiumsdiskussion: Future Perspectives in Cellular Therapies**. Novartis Expertenmeeting, November 22–23, 2018, Nürnberg, Germany

Köhl U. **From CAR T Cells to CAR Expressing NK Cells for Cancer Retargeting**. Haploidentical Transplant Symposium – HAPLO2018, November 29, 2018, San Diego, CA, USA

Köppen J, Schulze A, Wermann M, Guthardt M, Hähnel A, Menzel M, Klehm J, Demuth HU, Schilling S. **Impact of Amyloid-Beta on aggregation of alpha-synuclein**. 14. Research Festival Leipzig 2018, January 19, 2018, Leipzig, Germany

Körner S. **Development of an in vitro feeding system for modelling uptake and distribution of Coxiella burnetii in ticks**. Junior Scientist Symposium Friedrich-Loeffler-Institut (FLI) 2018, September 24–26, 2018, Greifswald - Insel Riems, Germany

Kretschmer A. **Immunonkologie - prädiktive Marker der Zukunft**. Jährliche Tagung des Berufsverbandes der niedergelassenen Onkologen (NIO Sachsen e.V.), November 3, 2018, Leipzig, Germany

Kubick S. **Cell-free Protein Synthesis**. Seminarreihe am Institut für Biotechnologie, Technische Universität Berlin, May 15, 2018, Berlin, Germany

Kubick S. **Cell-free Protein Synthesis**. Humboldt-Universität zu Berlin, Organische und Bioorganische Chemie, November 14, 2018, Berlin, Germany

Kubick S. **Cell-free synthesis and functional analysis of membrane proteins and glycoproteins**. Annual Congress Biotechnologie 2020+, October 4, 2018, Berlin, Germany

Kubick S. **Gesundheitswissenschaften**. Konferenz Lausitz 2030: Wissenschaft, Forschung und Kultur, BTU-CS, September 24, 2018, Cottbus, Germany

Kubick S. **Gesundheitswissenschaften – Perspektiven in der Lausitz Biotechnologie und Medizintechnik – Zukunftsfelder für die Region "Neue Bio-Technologien als Chance für die Region"**. Impulsvortrag an der Brandenburgischen Technischen Universität Cottbus-Senftenberg, July 18, 2018, Cottbus, Germany

Kubick S. **Identification of novel Antimicrobials using Cell-free Systems**. 11th Berlin Conference on Life Sciences: Novel Antimicrobials and AMR Diagnostics, March 2, 2018, Berlin, Germany

Kubick S. **Synthesis of membrane proteins and glycoproteins in eukaryotic cell-free systems**. Charité - Universitätsmedizin Berlin, Experimentelle Neurologie, Klinik und Poliklinik für Neurologie, June 13, 2018, Berlin, Germany

Kubick S. **Zellfreie Bioproduktion**. Seminar des Friedrich-Loeffler-Institut Bundesforschungsinstitut für Tiergesundheit, February 6, 2018, Greifswald - Insel Riems, Germany

Kubick S. **Zellfreie Proteinsynthese**. Beuth Hochschule, October 25, 2018, Berlin, Germany

Kubick S. **"Vom Gen zum Prozess zum Produkt: Zellfreie Proteinsynthese."** Processnet Jahrestagung der DECHEMA, September 10, 2018, Aachen, Germany

Kubick S. **Zellfreie Proteinsynthese**. Deutsches Institut für Ernährungsforschung, June 18, 2018, Potsdam-Rehbrücke, Germany

Kuhlmeier D. **Diagnostics meets material – why surface matters**. Bio meets material Fraunhofer IKTS, August 8, 2018, Dresden, Germany

Kuhlmeier D. **Infektionserregerdiagnostik am Fraunhofer-Institut für Zelltherapie und Immunologie IZI**. InfectoGnostics 2025: Vor-Ort-Diagnostik von Infektionen – gemeinsam neu gedacht InfectoGnostics Forschungscampus Jena, October 30, 2018, Jena, Germany

Kuhlmeier D. **Pathways from invasive to non-invasive medical diagnostics**. Besuch Universität Tartu, January 25, 2018, Tartu, Estland

Kuhlmeier D. **Point of care**. EU workshop TITTAN Workshop, February 6, 2018

Lang B, Glaser J, Stahl L, Müller A, Dluczek S, Wurm A, Hilger N, Kretschmer A, Behre G, Fricke S. **The role of specific microRNAs in immune cells and their functional effect in the immunological anti-tumor response**. Translational Immunology School, March 14–17, 2018, Potsdam, Germany

Lausch H, Fabian C, Brand M, Arnhold M, Hensel E, Rotsch C, Töppel T. **Mechanotransduktive Funktionalisierung von Implantatoberflächen**. 13. ThGOT: Oberflächen in der Medizintechnik 11. Thüringer Biomaterial-Kolloquium, March 13–15, 2018, Zeulenroda-Triebes, Germany

Laux EM, Gibbons J, Ermilova E, Bier FF, Hölzel R. **Dielectric spectroscopy of bovine serum albumin at GHz frequencies**. DPG-Frühjahrstagung, March 11–16, 2018, Berlin, Germany

Laux EM, Knigge X, Wenger C, Bier FF, Hölzel R. **AC electrokinetic manipulation of nanoparticles and molecules**. DPG-Frühjahrstagung, March 11–16, 2018, Berlin, Germany

Laux EM, Wenger C, Bier FF, Hölzel R. **Dielectrophoresis of organic fluorescence dye molecules**. Dielectrophoresis 2018, July 23–25, 2018, Guildford, Great Britain

Laux EM, Wenger C, Bier FF, Hölzel R. **Dielectrophoretic Immobilization of Nano-objects as Singles**. DPG-Frühjahrstagung, March 11–16, 2018, Berlin, Germany

Laux EM, Wenger C, Bier FF, Hölzel R. **Molecular AC electrokinetics using interdigitated electrodes**. DPG-Frühjahrstagung, March 11–16, 2018, Berlin, Germany

Leya T, Jorde F, Wenzel D, Teufelhart C, Lutz S, Benning L G, Merchant S, Gallaher S, Castruita M, Schmutz J. **Psychrophilic snow algae - their potential in biotechnology**. 2nd SAM2018, November 15–16, 2018, Potsdam, Germany

Leya T. **Psychrophilic snow algae: Model organisms for drougth and salt stress**. Workshop C. merolae as an emerging model organism, October 8–9, 2018, Berlin, Germany

Leya T. **From a snow algae biobank to industrial applications**. MPI-MP Institute Days, June 6–7, 2018, Potsdam, Germany

Lindner N, Krause J, Holm J, Kleymann G, Grunwald T. **Effectivity of novel antiviral therapy against human Herpes Simplex Virus (HSV) in an infection lethal challenge mouse mode**. 28th Annual Meeting of the Society for Virology, March 14–17, 2018, Würzburg, Germany

Lindner N, Krause J, Kleymann G, Grunwald T. **Efficacy of novel antiviral therapy against human HSV in an infection lethal challenge mouse model**. 17th Workshop Immunobiology of Viral Infections, September 26–28, 2018, Tauberbischofsheim, Germany

Lorenz J, Schnauß J, Glaser M, Sajfutdinow M, Schuldt C, Käs J, Smith D. **DNA-based biomimetics as tools to study reconstituted and cellular systems**. 15th Annual Conference on Foundations of Nanoscience: Self-assembled Architectures And Devices (Fnano18), April 16–19, 2018, Snowbird UT, USA

Lubitz T, Mükusch S, Seitz H. **Labelfree detection of in vitro Phosphorylation**. International Biotech Innovation Days, May 23–25, 2018, Senftenberg, Germany

Lubitz T, Mükusch S, Seitz H. **Labelfree detection of in vitro Phosphorylation**. Annual Congress Biotechnology 2020+, October 4, 2018, Berlin, Germany

Machner L, Schulze A, Wermann M, Köppen J, Hähnel A, Klehm J, König S, Demuth HU, Schilling S. **The effect of N-terminal truncations and pyroglutamate formation on fibril growth in Parkinson's disease**. 14. Research Festival Leipzig 2018, January 19, 2018, Leipzig, Germany

Makert G. **Development of an in vitro feeding system for the analysis of the vector capacity of ticks in the transmission of Coxiella burnetii**. 5. Jenaer Q-Fieber-Workshop: Friedrich-Loeffler-Institut (FLI), September 27–28, 2018, Jena, Germany

Makert G. **Development of an in vitro feeding system for the analysis of the vector capacity of ticks in the transmission of Coxiella burnetii**. Workshop on Arthropod-Borne Diseases, Friedrich-Loeffler-Institut (FLI), November 15–16, 2018, Greifswald - Insel Riems, Germany

Makert G. **Project Q-GAPS – The meaning of ticks for the transmission of Coxiella burnetii**. Highly virulent agents and their vectors, May 15–17, 2018, Komorni Hradek, Czech Republic

Marques L, Naaldijk Y, Fabian C, Stolzing A. **Cellular therapy for Alzheimer's disease**. Alzheimer's research UK, March 20–21, 2018, London, Great Britain

Memczak H, Hovestädt M, Ay B, Sänger S, Grzegorzewski J, König M, Wolff T, Bier FF. **Subtyping of influenza viruses using a peptide-based biosensing platform (FluType)**. BIOS 2018, January 27–29, 2018, San Francisco, USA

Menger M. **Aptamers - areal alternative to antibodies!** Seminar Fraunhofer ITEM, January 31, 2018, Hannover, Germany

Menger M. **Binding affinity analysis of DNA aptamers for therapeutic anthracyclines**. Aptamer 2018, April 12, 2018, Oxford, Great Britain

Menger M. **Generation of aptamers by in vitro selection**. Analytica - Session: Aptamer-based Biosensors, April 10, 2018, Munich, Germany

Menger M. **Sequence analysis & Interaction analysis**. Aptamer Workshop 2018 Universität Bonn, September 20, 2018, Bonn, Germany

Menger M. **Specific molecular recognition by aptamers!** Univercells, May 17, 2018, Gosselies, Belgium

Menger M. **Specific molecular recognition by aptamers!** fzmb GmbH, October 23, 2018, Bad Langensalza, Germany

Menger M. **Specific molecular recognition by aptamers!** Seminar Labor L+S, February 16, 2018, Bad Bocklet, Germany

Menger M. **Specific molecular recognition by aptamers!** Seminar Macherey & Nagel, August 15, 2018, Düren, Germany

Mitzner S. **Extracorporeal therapy of sepsis: Update and perspective**. Congress of the Japanese Society of Intensive Care Medicine, February 21, 2018, Chiba, Japan

Mitzner S. **Extracorporeal cytokine adsorption by hemoadsorbent polymer beads in sepsis management: International experience**. AVATAR Congress, June 22, 2018, New Delhi, India

Mitzner S. **Extracorporeal treatment of sepsis**. 38. ISICEM Congress, March 20, 2018, Brussels, Belgium

Mitzner S. **Role of Immune adsorption in the treatment of sepsis**. AKI & CRRT Congress, March 8, 2018, San Diego, USA

Mollenkopf P, Lorenz J, Glaser M, Käs J, Schnauß J, Smith D. **Friction in isotropic polymer networks**. 3rd Soft Matter Day, July 6, 2018, Leipzig, Germany

Mollenkopf P, Lorenz J, Glaser M, Käs J, Schnauß J, Smith D. **Friction in isotropic polymer networks**. 9th Annual Symposium "Physics of Cancer", September 25, 2018, Leipzig, Germany

Mollenkopf P, Lorenz J, Glaser M, Käs J, Schnauß J, Smith D. **Friction in isotropic polymer networks – "A science friction story"**. PWM Winterschool, February 26 – March 4, 2018, Vítkovice, Czech Republic

Möser C, Roderfeld E, Lauster D, Smith DM. **Trimeric DNA nanostructures as oligovalent carrier for peptides**. Soft Matter Day, July 6, 2018, Leipzig, Germany

Möser C. **DNA nanostructures as Oligovalent carriers for peptides**. DNA Mitteldeutschland Workshop, May 24, 2018, Jena, Germany

Möser C. **Using DNA nanostructures to present and potentiate peptides in an oligovalent manner**. PhD Workshop on Bioanalysis, November November 22–23, 2018, Luckenwalde, Germany

Möser C. **Using DNA nanostructures to present and potentiate peptides in an oligovalent manner**. 3rd Functional DNA Nanotechnology Workshop, June 6–8, 2018, Rome, Italy

Mükusch S, Knape M, Seitz H, Herberg F. **Unravelling antibody specifity employing multiple complementary approaches**. xMAP Connect, November 6–7, 2018, Amsterdam, The Netherlands

Mükusch S, Knape M, Seitz H, Herberg F. **Unravelling antibody specifity employing multiple complementary approaches**. Annual Congress Biotechnology 2020+, October 4, 2018, Berlin, Germany

Mükusch S, Rümpel E. **Lebensmittelsensor zur Sicherung von Qualität und Genießbarkeit**. Symposium Netzwert : Ideenwettbewerb "Mashup – gut gemischt ist halb gewonnen!", February 27–28, 2018, Munich, Germany

Nasiri AH, Künne S, Menger M, Mayer G. **The center of aptamer research and development**. Aptamer 2019, April 11–12, 2018, Oxford, Great Britain

Nasiri AH, Künne S, Menger M, Mayer G. **The center of aptamer research and development**. GBM-Tagung RNA Biochemistry, October 4–7, 2018, Bonn, Germany

Neumann M, Bier FF, Gajovic-Eichelmann N. **Ein neuer Schnelltest für Troponin I**. 19. Heiligenstädter Kolloquium, September 24–26, 2018, Heilbad Heiligenstadt, Germany

Nitzsche B, Hainsworth A, Bridges L, Zille M, Lobsien D, Barthel H, McLeod D, Gräßer F, Schatzl AK, Pietsch S, Dreyer AY, Boltze J, Ferrara F. **Lesional and perilesional tissue characterization by automated image procession in a novel gyrencephalic animal model of peracute intracerebral hemorrhage**. 10th International Symposium on Neuroprotection and Neurorepair, October 9–11, 2018, Radebeul, Germany

Otto D. **MCMC of Dynamical Systems as Uncertainty Propagation of qPCR Data**. 12th Annual Meeting of the Bompfünewerer Consortium, February 11–18, 2018, Bled, Slowenia

Rahfeld JU, Gnoth K, Piechotta A, Barendrecht S, Eichentopf R, Nykiel V, Demuth HU, Cynis H, Schilling S. **An Isoaspartate-Aβ specific antibody attenuates Alzheimer's Disease-like pathology and behavioral deficits in 5xFAD transgenic mice**. SfN - Neuroscience 2018, November 3–7, 2018, San Diego, USA

Rahfeld JU, Gnoth K, Piechotta A, Barendrecht S, Eichentopf R, Nykiel V, Demuth HU, Cynis H, Schilling S. **Monoclonal antibodies targeting isoaspartate-modified amyloid peptides**. 10th International Symposium on Neuroprotection and Neurorepair, October 9–11, 2018, Radebeul, Germany

Rahfeld JU, Gnoth K, Piechotta A, Kleinschmidt M, Nykiel V, Cynis H, Demuth HU, Schilling S. **Targeting Isoaspartate-modified Aβ: A Differential Approach of Passive Immunotherapy**. AAIC (Alzheimer's Association International Conference), July 22–26, 2018, Chicago, USA

Ramírez Caballero L, Puder M, Delaroque N, Wehrmann D, Fischer M, Szardenings M. **Mapping the antibody response to hepatitis B and influenza vaccinations direct from patient sera**. PepTalk, January 8–12, 2018, San Diego, USA

Ramm F. **Cell-free protein synthesis as a new platform technology for toxin synthesis and functional characterization**. 3rd German Pharm-Tox Summit, February 26 – March 1, 2018, Göttingen, Germany

Ramm F. **Synthesis and functional characterization of toxins using cell-free systems as a novel protein production platform**. Statusseminar des glyconet Berlin Brandenburg e.V., April 26, 2018, Potsdam-Golm, Germany

Ramsbeck D, Hamann A, Schlenzig D, Schilling S, Buchholz M. **Towards selective inhibitors of the astacin proteases Meprin alpha and beta**. 255th ACS National Meeting, March 18–22, 2018, New Orleans, USA

Ramsbeck D, Hamann A, Schlenzig D, Schilling S, Buchholz M. **Towards selective inhibitors of the astacin proteases Meprin alpha and beta**. HDDC 2018 – International Helmholtz Drug Discovery Conference, April 26–27, 2018, Munich, Germany

Raue C,Mükusch S, Seitz H. **Is your data normally distributed?** xMAP Connect, November 6–7, 2018, Amsterdam, The Netherlands

Rautenberger P, Ueberham E, Lehmann J. **Development of a test system based on monoclonal antibodies for the detection of allergenic food ingredients made of lupin proteins**. FAAM, October 18–21, 2018, Copenhagen, Denmark

Rautenberger P, Ueberham E, Lehmann J. **Development of test systems based on monoclonal antibodies for the detection of allergenic food ingredients produced from legume family proteins**. 14. Research Festival for Life Science, January 19, 2018, Leipzig, Germany

Rockstroh A, Ulbert S. **Specific serological diagnosis of dengue and Zika virus infections using recombinant envelope proteins**. Second International Conference on Zika Virus and Aedes Related Infections, June 14–17, 2018, Tallinn, Estonia

Rudolf D, Burkhardt J. **Relevance of immune checkpoint signals in NK cells**. 14. Research Festival Leipzig 2018, January 19, 2018, Leipzig, Germany

Sabrowski W, Klevesath A, Czepluch D, Rauch F, Dreymann N, Menger M. **Aptamers as specific recognition elements**. Fraunhofer Medizintechniktag, FHG Forum, September 12, 2018, Berlin, Germany

Sabrowski W. **Aptamerbasierte Biomarker-Assayentwicklungen**. Fraunhofer Matching Day 2018, September 20, 2018, Potsdam, Germany

Sajfutdinow M, Jacobs W, Reinhardt A, Smith D. **Nucleation and Growth of Brick Assembly**. DNA Mitteldeutschland, November 16, 2018, Potsdam, Germany

Sajfutdinow M. **Title DNA templated nanoprinting of functional surfaces**. Defense Talk, August 14, 2018, Leipzig, Germany

Sandetskaya N. **Development of a versatile lab-on-a-chip system for molecular diagnostics of infections**. Research on live systems in post-genomic era, Staatliche Universität Wolgograd, May 18, 2018, Volgograd, Russia

Sandetskaya N. **Lab-on-Chip for rapid molecular diagnostics of bacterial infections**. 28. Jahrestagung der Gesellschaft für Kinder- und Jugendrheumatologie (GKJR) und 34. Jahrestagung der Arbeitsgemeinschaft Pädiatrische Immunologie (API), May 4, 2018, Innsbruck, Austria

Sänger S, Memczak H, Hovestädt B, Ay B, Bier FF, Wolff T. **FluType – Development of a peptide based finetyping platform for influenza A viruses**. 28th Annual Meeting of the Society for Virology, March 14–17, 2018, Würzburg, Germany

Sass S, Stöcklein WF, Klevesath A, Hurpin J, Hille C, Menger M. **Binding affinity analysis of DNA aptamers for therapeutic anthracyclines**. Aptamer 2018, April 12, 2018, Oxford, Great Britain

Sass S, Stöcklein WF, Klevesath A, Hurpin J, Menger M, Hille C. **Binding affinity data of DNA aptamers for therapeutic anthracyclines from microscale thermophoresis and surface plasmon resonance spectroscopy**. GBM-Tagung RNA Biochemistry, October 4–7, 2018, Bonn, Germany

Sass S, Stöcklein WF, Klevesath A, Hurpin J, Menger M, Hille C. **Binding affinity data of DNA aptamers for therapeutic anthracyclines from microscale thermophoresis and surface plasmon resonance spectroscopy**. Aptamers in Boulder, August 3–4, 2018, Boulder, USA

Schieke K, Echtermeyer D, Pliquett U, Martin D, Frense D, Beckmann D, Menger M, Reichl M, Dohndorf R, Liebold F, Sachse A. **Aptasensor für Arzneimittelreststoffe in Klärwerksabwässern nach der 4**. Reinigungsstufe auf Basis der schnellen Impedanzspektroskopie. 19. Heiligenstädter Kolloquium, September 24–26, 2018, Heilbad Heiligenstadt, Germany

Schlimper R, Zürner S, Hering A, Wagner T, Braumann UD. **Determination of Fibre Lengths in Glass Fibre Reinforced Injection Moulding Material via X-Ray Computed Tomography**. PolyMerTec18: Internationale wissenschaftliche Tagung Polymerwerkstoffe, June 13–15, 2018, Hochschule Merseburg, Germany

Smith D. **Bottom-up engineering of nanoscale devices**. Leibniz-Institut für Photonische Technologien e.V. Spring Workshop, April 20, 2018, Leipzig, Germany

Smith D. **Bottom-up engineering of nanoscale devices to program macroscopic material properties**. Invited Lecture, Jawaharlal Nehru Centre for Advanced Scientific Research, December 13, 2018, Bangalore, India

Smith D. **Bottom-up engineering of nanoscale devices to program macroscopic material properties**. Invited Lecture, Dhirubhai Ambani Institute of Information and Communication Technology, December 17, 2018, Gandhinagar, India

Smith D. **Studying nucleation and mechanics of macromolecules with DNA-based mimics**. Invited Lecture, Universität Paderborn, October 19, 2018, Paderborn, Germany

Stanke S, Wenger C, Bier FF, Hölzel R. **AC field assisted deposition of antibodies for virus detection**. DPG-Frühjahrstagung, March 11–16, 2018, Berlin, Germany

Stanke S, Wenger C, Bier FF, Hölzel R. **Biosensor surface functionalization based on AC electrokinetic forces**. Dielectrophoresis 2018, July 23–25, 2018, Guildford, Great Britain

Stech M. **Antibody production and modification using a eukaryotic cell-free system based on CHO cell lysates**. BIO, June 1–7, 2018, San Francisco, USA

Stech M. **Entwicklung und Produktion von Antikörper-Toxin-Konjugaten mittels zellulärer und zellfreier Proteinsynthese**. Statusseminar des glyconet Berlin Brandenburg e.V., April 26, 2018, Potsdam-Golm, Germany

Stech M. **Synthesis and modification of antibodies in eukaryotic cell-free systems**. Statusseminar des glyconet Berlin Brandenburg e.V., April 26, 2018, Potsdam-Golm, Germany

Steppert C, Dick T, Steppert I, Becher G, Bollinger T. **Rapid in vitro diagnostic of Bacterial Species by MCC-IMS**. ATS 2018 International Conference, May 18–23, 2018, San Diego, USA

Steppert C, Dick T, Steppert I, Bollinger T, Becher G. **Rapid in vitro detection of resistant strains by MCC-IMS**. ERS International Congress 2018, September 15–19, 2018, Paris, France

Szardenings M. **Antibody epitopes alive**. Bionection, October 24–25, 2018, Dresden, Germany

Szardenings M. **FoodAllergen: Ein holistischer Ansatz bei Lebensmittelallergien**. Fraunhofer Netzwert Symposium, February 27–28, 2018, Munich, Germany

Szardenings M. **Mapping the human immunome response: Time and amino acid level resolved epitopes**. Charité – Universitätsmedizin Berlin, August 21, 2018, Berlin, Germany

Szardenings M. **Personalized immune diagnostics from high resolution mapping of the human immunome**. Wonju Medical Industry Technovalley, Yonsei University, September 5, 2018, Wonju, South Korea

Szardenings M. **Rapid and extensive epitope fingerprinting of mono- and polyclonal antibodies**. Nano Seminar Series, Institute for Materials Science and Max Bergmann Center of Biomaterials, Technische Universität Dresden, March 9, 2018, Dresden, Germany

Szardenings M, Eisner P, Weisz U, Ueberham E, Lehmann J, Ehrentreich-Förster E, Schillberg S. **FoodAllergen: A joint Fraunhofer Project handling food ingredients, allergens and allergies**. ILSI-Symposium on Frontiers in Food Allergy and Allergen Risk Assessment and Management, April 18–20, 2018, Madrid, Spain

Tan K, Ramsbeck D, Schlenzig D, Schilling S, Demuth HU, Buchhholz M. **Towards selective inhibitors of Meprin alpha**. 35th Winterschool on Proteinases and Inhibitors, February 28 – March 4, 2018, Tiers, Italy

Thoring L, Stech M, Knauer JF, Zemella A, Wüstenhagen DA, Kubick S. **Flexible High Yield Production of "Difficult-to-Express" Proteins using CHO cell-free systems**. Annual Congress Biotechnologie 2020+, October 4, 2018, Berlin, Germany

Thoring L, Jorde F. **Photo-CHO ein neuartiges Lichtinduzierbares Proteinexpressionssystem**. Kurzpitch zur Projektidee vor Industriepublikum im Rahmen der Fraunhofer LifeScience FDays 2018, September 19, 2018, Göttingen, Germany

Thoring L, Jorde F. **Photo-CHO ein neuartiges Lichtinduzierbares Proteinexpressionssystem**. Pitch zur Projektidee vor Industriepublikum im Rahmen der Fraunhofer LifeScience FDays 2018, December 6, 2018, Göttingen, Germany

Thoring L, Kubick S. **Cell-free Protein Synthesis**. Technische Universität Berlin, Fakultät III – Prozesswissenschaften, Institut für Biotechnologie, Fachgebiet Bioverfahrenstechnik, May 5, 2018, Berlin, Germany

Thoring L, Rosencrantz RR, Palkowitz A, Böcker S, Stiller S, Böker A, Kubick S. **Glycopolymer based surfaces: A novel and gentle detachment technology for adherent cells**. Annual Congress Biotechnologie 2020+, October 4, 2018, Berlin, Germany

Thoring L. **CHO cell-free protein synthesis for mammalian protein production and future bioprocess development**. BioProScale, March 20–22, 2018, Berlin, Germany

Thoring L. **Eukaryotic Cell-free systems based on Chinese Hamster ovary cells for the production of glycoproteins and membrane proteins**. Statusseminar des glyconet Berlin Brandenburg e.V., April 26, 2018, Potsdam-Golm, Germany

Thoring L. **Novel Glycopolymer based surface coatings for the cultivation and smooth detachment of adherent cells**. Statusseminar des glyconet Berlin Brandenburg e.V., April 26, 2018, Potsdam-Golm, Germany

Ueberham E, Murany I, Havenith H, Spiegel H, Rautenberger P, Lidzba N, Weisz U, Schillberg S, Eisner P, Lehmann J. **Setting the demarcation line of legume crops – Assays for detecting and quantifying pea proteins**. FAAM, October 18–21, 2018, Copenhagen, Denmark

Ueberham E, Spiegel H, Havenith H, Rautenberger P, Lidzba N, Schillberg S, Lehmann J. **Reliable detection of soy protein in processed food by several sets of monoclonal antibodies against particular allergenic proteins**. FAAM, October 18–21, 2018, Copenhagen, Denmark

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GRADUATION (CLASS OF 2018)

Alkhashrom, Sewar. **Characterization of the substrate spectrum of the zebrafish uptake transporter Oatp1d1**. Martin Luther University Halle-Wittenberg, Master thesis

Ayash, Mohamed Adel Abdelaziz. **Cloning and heterologous expression of human Ovastacin in *E. coli, P. pastoris* and *Drosophila S2* cells.** Martin Luther University Halle-Wittenberg, Master thesis

Bayer, Lea. **Novel approaches towards an RSV vaccine: Papillomavirus-based delivery of a genetic vaccine and low-energy electron irradiation for the production of a killed vaccine**. Martin Luther University Halle-Wittenberg, Doctoral thesis

Berneck, Beatrice. **Inaktivierungsmethoden mittels Elektronenbestrahlung und chemischer Behandlung im Vergleich von Zika-Viren**. Leipzig University, Master thesis

Danckert, Lena. **Immunscreening Virulenz-adaptierter Expressionsbibliotheken aus einem in vitro Infektionsmodell mit *Salmonella* Enteritidis**. University of Potsdam, Doctoral thesis

Danne, Denise. **Methoden zum quantitativen Nachweis von Bakterien in Kerosin-Wasser-Gemischen**. Technical University of Applied Sciences Wildau, Bachelor thesis

Dluczek, Sarah. **Purification and Characterization of New Antimicrobial Phytosubstances (AMPS) from *Warburgia ugandensis***. University of Ulm and Biberach University of Applied Sciences, Master thesis

Donner, Anne-Kathrin. **Wirksamkeitstestung des Helikase-Primase Inhibitors PXI26250 gegen das Herpes simplex Virus Typ 1**. Mittweida University of Applied Sciences, Bachelor thesis

Engberg, Diana. **Analyse der Toxizität und antiviralen Aktivität von Inhibitoren gegen das Respiratorische Synzytial Virus**. Leipzig University, Master thesis

Enssle, Deborah. **Der Einfluss von Urämietoxinen und deren Vorstufen auf humane intestinale Epithelzellen in vitro**. University of Rostock, Bachelor thesis

Gehre, Christian. **Echtzeitcharakterisierung verschiedener Hepatozyten in einem neuartigen Mikrobioreaktor**. Philipps-Universität Marburg, Master thesis

Golusda, Laura. **Characterization of different isolation strategies for prostate cancer-derived extracellular vesicles**. Freie Universität Berlin, Master thesis

Görner, Christian. **Entwicklung eines Testsystems zur Bestimmung der Hämokompatibilität kardiovaskulärer Implantate unter kontrollierten hydrodynamischen Bedingungen**. Martin Luther University Halle-Wittenberg, Master thesis

Hantel, Friederike. **Expression, Reinigung und Charakterisierung monoklonaler Antikörper gegen posttranslational modifizierte Varianten des Aβ Peptides**. Martin Luther University Halle-Wittenberg, Master thesis

Haueis, Lisa. **Etablierung von Verfahren zur Bead-basierten, funktionellen Charakterisierung von Membranproteinen aus eukaryotischen zellfreien Systemen**. Beuth University of Applied Sciences Berlin, Master thesis

Haupt, Susan. **Development of a 3D printed microdevice for detection of peptide epitope specific antibodies in blood serum**. Technische Universität Dresden, Master thesis

Hebel, Nicole. **Vergleichende Charakterisierung prokaryotischer und eukaryotischer zellfreier Systeme für die Herstellung und ortsspezifische Markierung von Membranproteinen**. University of Potsdam, Master thesis

Hoffmann, Maximilian. **Immunmodulierende Wirkungen von Pflanzeninhaltsstoffen bei chronisch-entzündlichen Darmerkrankungen im experimentellen Mausmodell**. Leipzig University, Doctoral thesis

Horn, Katharina. **Etablierung von Potency-Assays für einen monoklonalen anti-hCD4-IgG4-Antikörper im Rahmen der Qualitätskontrolle**. Ernst-Abbe-Hochschule Jena (EAH), University of Apllied Sciences, Master thesis

Kaipa, Jagan Mohan. **Experimental investigation on susceptibility of cancer cells to small weight phytocompounds Silibinin and Withaferin-A**. Martin Luther University Halle-Wittenberg, Master thesis

Kersting, Sebastian. **Isothermal nucleic acid amplification for the detection of infectious pathogens**. University of Potsdam, Doctoral thesis

Knauer, Jan-Felix. **Cell-free synthesis of virus-like particles: Functional characterization of Coxsackievirus and Adenovirus receptor ligands**. Freie Universität Berlin, Master thesis

Kny, Christoph. **Epitopes of natural allergens recognized by patient sera with respect to seasonal variation**. Brandenburg University of Technology Cottbus-Senftenberg, Master thesis

Krüger, Anneliese. **Fluoreszenzmarkierung und Charakterisierung der poren-bildenden Toxine α-Hämolysin und Aerolysin in zellfreien Systemen**. Beuth University of Applied Sciences Berlin, Master thesis

Lehrer, Christina. **Kinome Profiling and Peptide Substrate reporter Maturation of tonic and activated B cell receptor pathway on in situ synthesized peptide microarrays**. Heidelberg University, Doctoral thesis

Lorenz, Jessica. **DNA-based biomimetics as modular tools to study reconstituted and cellular systems**. University of Cologne, Doctoral thesis

Ludwig, Charlott. **Heterologous expression of LOXL2 in *P. pastoris* and human procollagen III in *E. coli*.** Martin Luther University Halle-Wittenberg, Master thesis

Machner, Lisa. **Expression, Reinigung und Charakterisierung von modifiziertem a-Synuclein**. Martin Luther University Halle-Wittenberg, Master thesis

Meier, Stefanie. **Rekombinante Expression von Antikörpern gegen posttranslationale modifizierte Formen des Abeta-Peptids**. Martin Luther University Halle-Wittenberg, Bachelor thesis

Mirtschink, Bianca. **Bildgebungsverfahren zur Analyse dreidimensionaler Strukturen**. Mittweida University of Applied Sciences, Bachelor thesis

Pallien, Tamara. **Entwicklung eines RNA-basierten diagnostischen Tests für *Chlamydia trachomatis***. Humboldt-Universität zu Berlin, Master thesis

Pellegrino, Antonio. **Influence of post-translational modifications on the activity of transcription factor CREB**. Fresenius University of Applied Sciences, Master thesis

Rahman, Masudur. **Role of alpha2a andrenoceptors in angiotensin II induced hypertensive nephropathy**. Martin Luther University Halle-Wittenberg, Master thesis

Redwanz, Catherina. **Modellentablierung zur Abbildung der Blut-Hirnschranken-Integrität**. University of Rostock, Bachelor thesis

Richter, Theresa. **Zellfreie Synthese des Adenosin A2a Rezeptors: Fluoreszenzmarkierung und Funktionsanalyse**. University of Potsdam, Master thesis

Rockstroh, Alexandra. **Entwicklung von Verfahren für die spezifische, serologische Diagnostik von Dengue- und Zika-Virusinfektionen mit modifizierten *Envelope* Proteinen**. Leipzig University, Doctoral thesis

Roderfeld, Eleonore. **DNA nanostructures as oligovalent carriers for an influenza virus-inhibiting peptide**. Brandenburg University of Technology Cottbus-Senftenberg, Bachelor thesis

Roman, Alexandra. **Untersuchung von scherinduzierten Blutreaktionen im Zuge von dynamischen Hämokompatibilitätstests an kardiovaskulären Implantaten**. Technische Universität Berlin, Bachelor thesis

Sajfutdinow, Martin. **DNA templated nanoprinting of functional surfaces**. Leipzig University, Doctoral thesis

Schatzl, Ann-Kathrin. **Wirksamkeitstestung von Helikase-Primase Inhibitoren bei Herpes simplex Virus Typ 2 (HSV-2) Infektionen**. Berufsakademie Sachsen - Staatliche Studienakademie Riesa, Bachelor thesis

Schmidt, Felix. **Durchflusszytometrische Analyse des Graft-versus-Leukämie-Effektes nach hämatopoetischer Stammzelltransplantation in Mäusen**. Leipzig University, Doctoral thesis

Schnack, Jan Philipp. **Standardisation of a manual leukocyte preparation procedure via development of a semi-automated pumping process**. Flensburg University of Applied Sciences, Master thesis

Scholz, Alexander. **NGS Data Analysis within the scope of molecular diagnostics**. Leipzig University, Master thesis

Scholz, Rebekka. **Vergleichende Expression und Reinigung von Hüllproteinen humaner endogener Retroviren in *Escherichia coli***. Martin Luther University Halle-Wittenberg, Bachelor thesis

Schuldt, Carsten. **Semiflexible Polymer Networks and Persistence Length**. Leipzig University, Doctoral thesis

Schumann, Conrad. **Phänotypisierung eines transgenen Alzheimer-Mausmodells - Charakterisierung und Vergleich von männlichen und weiblichen Tieren im Alter von 6 Monaten**. Martin Luther University Halle-Wittenberg, Bachelor thesis

Shahd, Fabian. **Etablierung von In-vitro-Methoden zum Nachweis der Tumorizidie therapeutischer monoklonaler Antikörper am Beispiel eines Glypican-1-Antikörpers**. Leipzig University, Diploma thesis

Tan, Kathrin. **Synthese und Charakterisierung neuartiger Meprin a-Inhibitoren**. Martin Luther University Halle-Wittenberg, Diploma thesis

Teichmann, Tamara. **Synthese und Charakterisierung ortsspezifisch markierter Antikörper in Zelllysaten basierend auf kultivierten CHO-Zellen**. University of Potsdam, Master thesis

Thate, Fabian. **Synthese und Charakterisierung neuartiger Meprin-Inhibitoren mit alternativer Zinkbindungsgruppe**. Leipzig Unversity, Diploma thesis

Yoluc, Yasmine. **The role of immune cells in Alzheimer's Disease**. Ludwig-Maximilians-Universität München, Master thesis

Zajac, Julia. **IgY antibodies against bacterial infection : Development of candidate IgY antibodies against ESBL-producing gram-negative bacteria for oral therapy**. Leipzig University, Doctoral thesis

Zürner, Sebastian. **Entwicklung eines Tools zur zerstörungsfreien 3D-Mikrostrukturanalyse faserverstärkter Kunststoffe**. Leipzig University of Applied Sciences (HTWK Leipzig), Master thesis

PRIZES AND AWARDS

Fraunhofer IZI publication prizes were awarded to Dr. Martin Sajfutdinow on the topic "Nanoscale patterning of self-assembled monolayer (SAM)-functionalised substrates with single molecule contact printing", to Tilo Buschmann on the topic "DNABarcodes: An R package for the systematic construction of DNA sample tags", and to Dr. Alexandra Rockstroh on the topic "Specific detection of dengue and Zika virus antibodies using envelope proteins with mutations in the conserved fusion loop".

Fraunhofer IZI Science Day poster prizes were awarded to Nadja Lindner on the topic "Effectivity of novel antiviral therapy against human Herpes simplex virus (HSV) type 1 & type 2 in an infection lethal challenge mouse model", to Paul Rautenberger on the topic "Development of test systems based on monoclonal antibodies for the detection of allergenic food ingredients produced from legume family proteins", and to Kathrin Tan on the topic "Synthesis and characterization of inhibitors of human astacin proteases".

Hugo Junkers Prize 2018 in the category "Most innovative foundational research project" (3rd place) was awarded by the Ministry of Economy, Science and Digitalisation of the Land of Saxony-Anhalt to Dr. Mirko Buchholz, Professor Hans-Ulrich Demuth and Dr. Stephan Schilling for the development of a highly specific antibiotic for treating periodontitis.

Prize awarded by Boehringer Ingelheim Pharma GmbH & Co. KG for an outstanding thesis on a Pharmaceutical Biotechnology degree course to Sarah Dluczek on the topic "Purification and Characterization of New Antimicrobial Phytosubstances (AMPS) from *Warburgia ugandensis*".

Speed lecture award (2nd place) handed to Christian Gehre on the topic "Liver on a chip" at the Bionnale Berlin 2018.

PATENTS

The patent portfolio of the Fraunhofer IZI currently holds 40* patent families which are available for use in cooperation projects as well as for direct commercialization and licensing.

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Fraunhofer IZI holds patent families in the following fields of technology:

- Technologies for generating pluripotent stem cells
- Procedures for diagnosing infecting agents
- Procedures for diagnosing cancerous diseases
- New treatment procedures for cancer and other diseases
- New procedure for preventing graft-versus-host-disease (GvHD)
- Method for immobilizing cells on surfaces
- Procedure for diagnosing dyslexia
- Methods for ascertaining liver function and regeneration
- Procedure for diagnosing chronic lung diseases
- Mineral compounds for the prevention / treatment of kidney and bowel diseases
- Methods of treating neurological and neuropsychological diseases
- Substrate, cultivation facility and cultivation procedures for biological cells
- Electrochemical detection methods for binding reactions
- Cell-free protein synthesis procedure
- Procedure for manufacturing zinc fingers and concatemers
- Coimmobilization of several chemical species
- Procedure for manufacturing transparent films from cellulose dispersions and their use as multifunctional ligand carriers
- Device for measuring luminescence
- Procedure for manufacturing a leukocyte preparation
- Development of antimicrobial peptides
- Treating neurogenic immunodepression following brain injuries
- Technologies for generating pluripotent stem cells
- Biomarkers and diagnostic systems for application in human or veterinary medicine
- RNA species for therapeutic and/or diagnostic use
- Treatment approaches for cancer
- Procedures and devices for point-of-care diagnostics
- Drugs for the treatment of infectious as well as fibrotic and neurodegenerative diseases
- Procedure for immunomodulation and treatment of immunological diseases
- Surface modification
- Inactivating pathogens as part of vaccine production and novel vaccine candidates
- Methods for transferring nucleic acids into cells
- Epitopes from food relevant to the development of allergies
- Procedure for transplanting microbiomes
- Components of microscopical systems, especially from light sheet microscopy
- Methods for ascertaining liver function and regeneration
- Mineral compounds for the prevention / treatment of kidney and bowel diseases
- Dialysis procedures and novel components of dialysis systems
- Biomarkers and diagnostic procedures for dyslexia based thereon

* without Fraunhofer IZI-BB patents

FURTHERANCE

SPONSORS AND ADVISORY BOARD OF THE FRAUNHOFER IZI

The support and commitment of active institutions and individuals enable the Fraunhofer IZI to experience continuous and successful development as well as dynamic growth.

Sponsors

The Fraunhofer IZI would like to thank the European Union, the Federal Ministry of Education and Research, the Free State of Saxony and the City of Leipzig via the Leipzig Foundation for Innovation and Technology Transfer for their financial support.

The European Union sponsors through the programs EFRE and ESF. The building projects of the Fraunhofer IZI are sponsored 60 percent by the European Union and 20 percent each by the Federal Ministry of Education and Research and the Free State of Saxony. The plot of land is provided by the City of Leipzig in hereditary leasehold and free of charge. Furthermore, Fraunhofer IZI would like to thank the Leipzig Foundation for Innovation and Technology Transfer for its support during the institute's construction phase from 2005 to 2010.

Advisory board

The advisory board functions as the external expert committee for strategic questions regarding the institutional direction and the Fraunhofer-Gesellschaft. Its members are invited and appointed by the president of the Fraunhofer-Gesellschaft. The advisory board includes representatives from industry and research as well as from authorities, ministries and foundations. The board meets once a year and evaluates the performance and image of the institute.

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THE FRAUNHOFER-GESELLSCHAFT IN PROFILE

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 72 institutes and research units. The majority of the more than 26 600 staff are qualified scientists and engineers, who work with an annual research budget of more than 2.5 billion euros. Of this sum, more than 2.1 billion euros is generated through contract research. Around 70 percent of the Fraunhofer-Gesellschaft's contract research revenue is derived from contracts with industry and from publicly financed research projects. Around 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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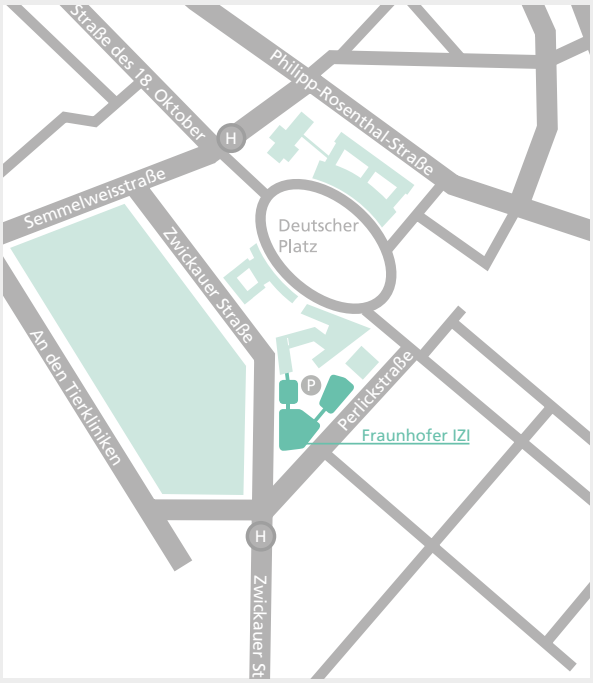

Address

Fraunhofer Institute for Cell Therapy and Immunology
Perlickstraße 1
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Germany

By car

A9 – Exit Leipzig-West: Take the B181 in the direction of the city center ("Zentrum") and follow the B87 (Merseburger Straße, Lützner Str., Jahnallee). After passing the central station, turn right towards Augustusplatz (Leipzig Opera House). At Augustusplatz turn left and keep to the right, then follow Prager Straße. Turn right at Semmelweissstraße, follow the road and then turn left onto Zwickauer Straße. Follow this road until you turn left into Perlickstraße.

A14 – Exit Leipzig-Mitte: Take the B2 (via Maximilianallee) in the direction of the city center ("Zentrum") and follow the B2 (via Gerichtsweg). Turn left onto Prager Straße (B2) in the direction of "Alte Messe", then turn right onto "Alte Messe". Turn right at Semmelweissstraße, follow the road and then turn left onto Zwickauer Straße. Follow this road until you turn left into Perlickstraße.

A38 – Exit Leipzig-Süd: Take the B2 in the direction of the city center ("Zentrum") and turn off at exit "Richard-Lehmann-Straße". Follow Richard-Lehmann-Straße and turn off before the BMW car dealership onto Zwickauer Straße in the direction of "Alte Messe", then turn right onto Perlick-straße.

The car park is accessible from Perlickstraße. You will find visitors' parking right in front of the façade of the institute.

By train and public transport

Take the train to Leipzig Hauptbahnhof central station, and then continue with tram line 16 towards Lößnig. Get off at the stop "An den Tierkliniken", directly opposite the institute. The closest overground train ("S-Bahn") station is "Leipzig MDR" and all overground trains stop there (10–15 minute walk to the institute).

From the airport

With the overground train ("S-Bahn") towards Leipzig Central Station, then follow the directions given under "Train and Public Transport".

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Translation
LSI World of Languages GmbH

Photo acknowledgements
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