




ANNUAL REPORT
2020

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**STRUCTURES &
FIGURES 2020**

PORTRAIT OF THE INSTITUTE

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 within the business fields cell and gene therapy, drugs and vaccines, molecular diagnostics and immunodiagnostics, as well as extracorporeal therapies. Its areas of competence lie in cell biology, immunology, drug biochemistry, bioanalytics and bioproduction as well as process development and automation. Research in these areas is centered around developments in immuno-oncology and infectious disease pathology. The S3 safety laboratory allows research and development activities to be conducted and highly pathogenic agents investigated under biosafety level 3 conditions.

The institute works in close cooperation with hospital institutions and performs quality tests besides manufacturing investigational medicinal products in line with GMP requirements. Furthermore, it supports partners in developing processes for the pharmaceutical production of ATMPs and biologicals, for example by helping them to obtain manufacturing licenses.

ORGANIZATION LEIPZIG HEADQUARTERS

DIRECTOR

Prof. Dr. Dr. Ulrike Köhl (geschäftsführend) | PD Dr. Sebastian Ulbert (deputy)

ADMINISTRATION

Anja Bochmann-Seidel | Annette Schäfer (deputy)

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. Franziska Lange
- Imaging and image analysis
Prof. Dr. Ulf-Dietrich Braumann
- GLP test facility
Dr. Jörg Lehmann

OFFICERS

MAIN DEPARTMENT OF GMP CELL AND GENE THERAPY

Dr. Gerno Schmiedeknecht |
Kati Kebbel

DEPARTMENT OF GMP PROCESS DEVELOPMENT / ATMP DESIGN

PD Dr. Stephan Fricke

DEPARTMENT OF PRECLINICAL DEVELOPMENT AND VALIDATION

Dr. Jörg Lehmann

- Preclinical Models,
Sina Riemschneider
- Protein Biomarker,
Prof. Dr. Stefan Kalkhof
- Cell Line Development,
Dr. Elke Ueberham
- Veterinary Pathology,
Dr. Anke Hoffmann

DEPARTMENT OF VACCINES AND INFECTION MODELS

PD Dr. Sebastian Ulbert |
PD Dr. Thomas Grunwald

- Vaccine Technologies,
Dr. Jasmin Fertey
- Preclinical Validation,
PD Dr. Thomas Grunwald
- Vector-based Immuno-
therapy, Prof. Dr. Hildegard
Büning | Prof. Dr. Ulrich
Hacker
- Infection Models and
Immunodiagnosics,
Dr. Franziska Lange
- Antimicrobial Agents,
Dr. Andreas Schubert
- Biological Material Analytics
(Fraunhofer IKTS ATTRACT-
Group), Dr. Juliane Spohn

DEPARTMENT OF DIAGNOSTICS

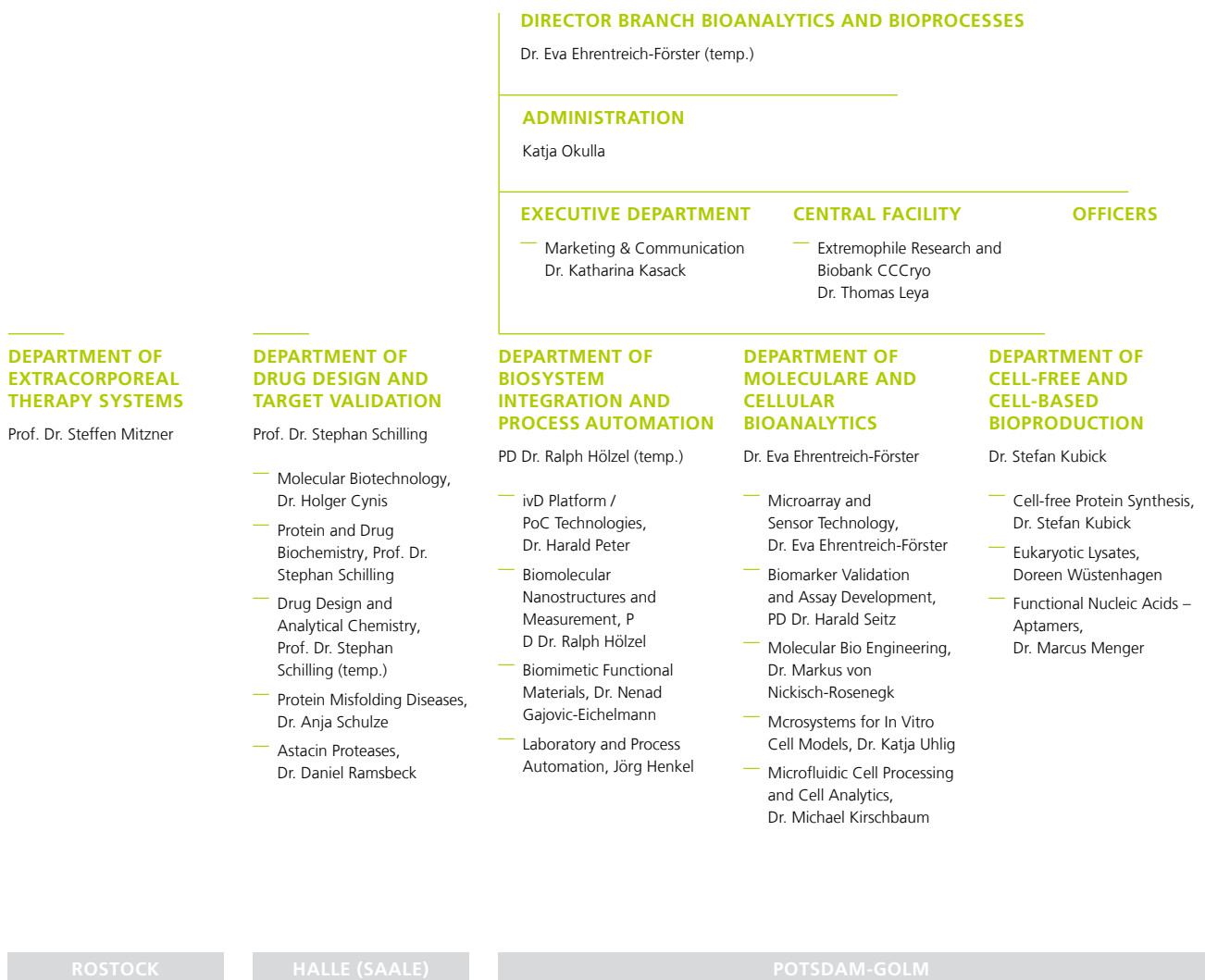
Dr. Dirk Kuhlmeier

- CardiOmics, Prof. Dr.
Dr. Dr. Andreas Oberbach
- Ligand Development,
Dr. Michael Szardenings
- Experimental Imaging,
Dr. Sebastian Greiser
- Image Analysis of Cell
Function, Prof. Dr.
Ulf-Dietrich Braumann
- MicroDiagnostics,
Dr. Dirk Kuhlmeier
- DNA Nanodevices,
Dr. David M. Smith
- Next-Generation
Diagnostics,
Dr. Conny Blumert
- Bioinformatics,
Dr. Kristin Reiche

HEADQUARTER LEIPZIG

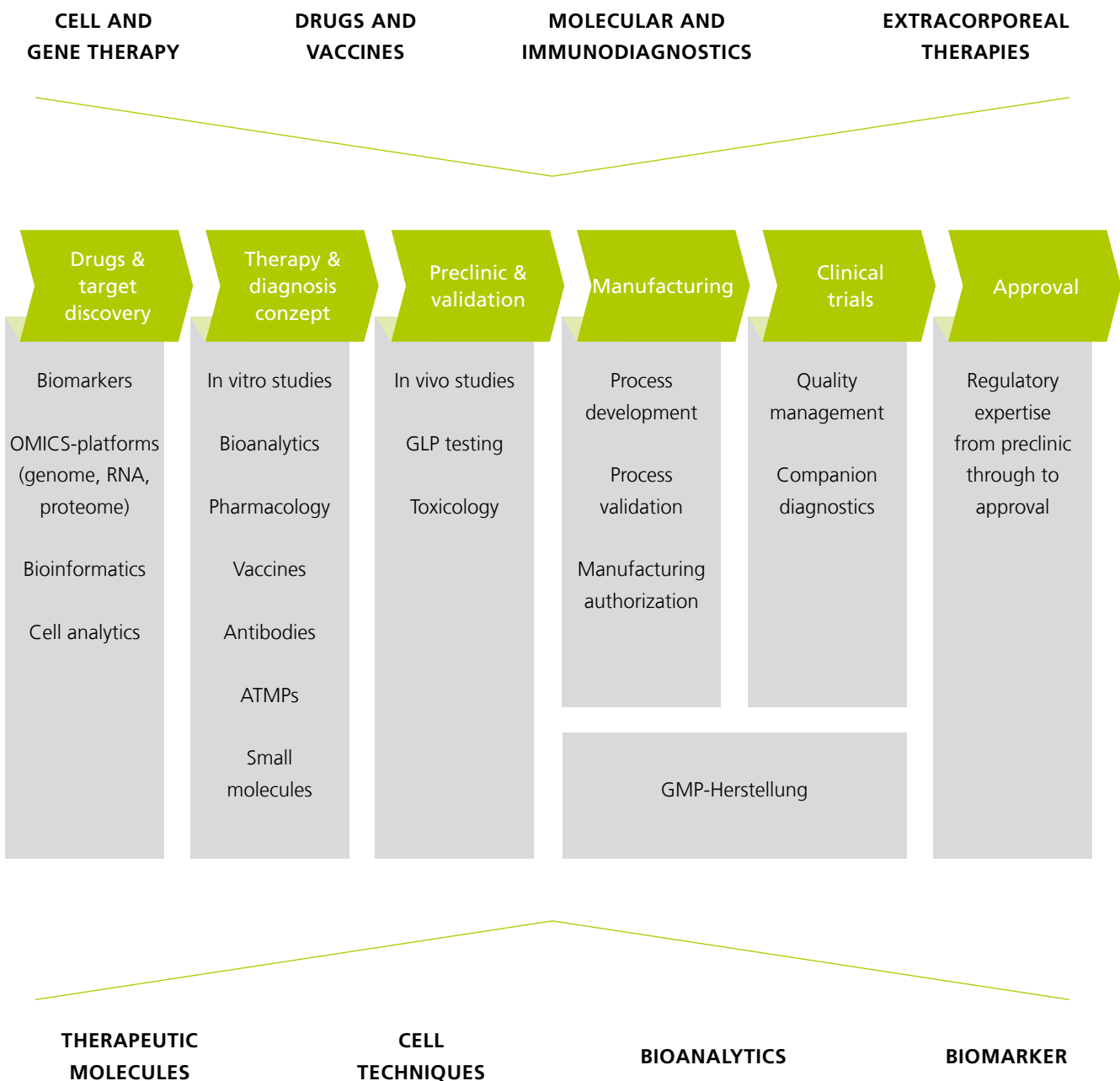
April 2021

ORGANIZATION BRANCHES



Stand April 2021

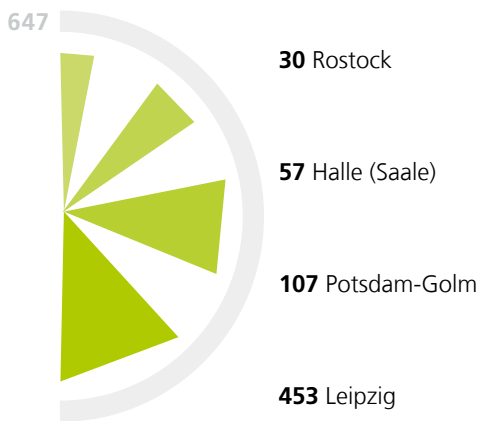
BUSINESS UNITS AND COMPETENCIES



KEY INSTITUTE FIGURES 2020

EMPLOYEES

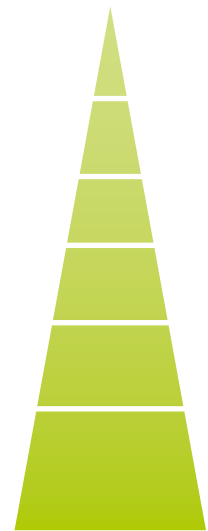
by location



EMPLOYEES

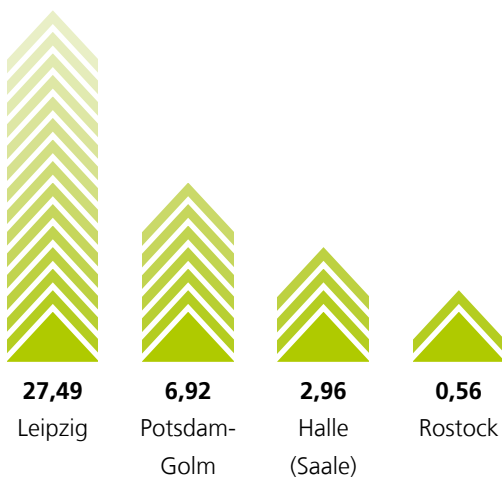
workforce composition

- 5 % Trainees / interns / diploma students / bachelor students / master students
- 8 % PhD students
- 10 % Student / scientific assistants
- 11 % Administration / executive departments / IT / technical infrastructure
- 19 % Technical assistants and laboratory technicians
- 47 % Research and technical engineering staff incl. guest researchers



37,9 MIO € PROJECT REVENUE

by location € mio



PROJECT REVENUE

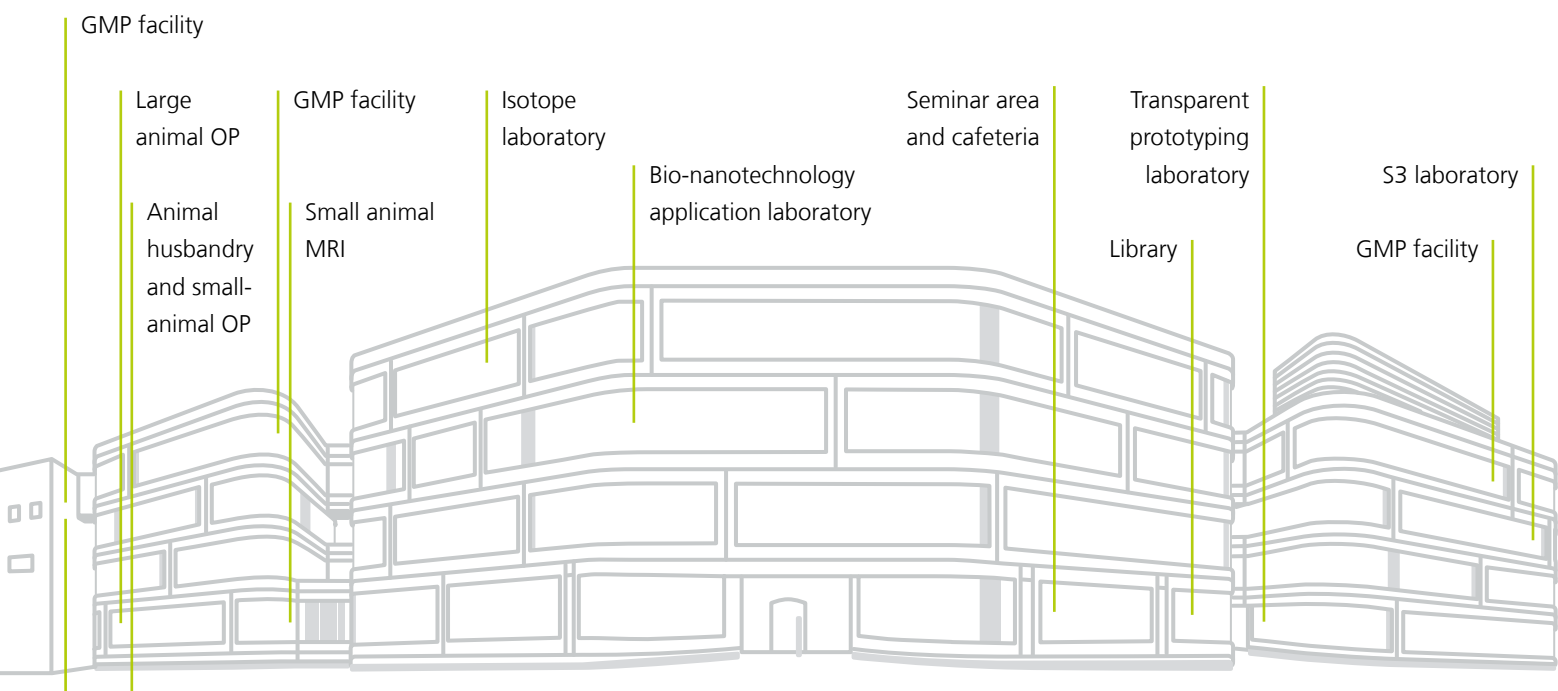
by funding agency

- 0,9 % EU (358 TEUR)
- 22,2 % Other (8 406 TEUR)
- 28,6 % German national and regional government (10 850 TEUR)
- 48,3 % Industry (18 315 TEUR)



December 31, 2020

RESEARCH INFRASTRUCTURE AT THE LEIPZIG SITE



FIRST EXTENSION BUILDING

Start-up operations: 2012
 Usable area: 1 568 m²
 Lab space: 470 m²
 Offices: 142 m²
 Clean rooms: 410 m²

MAIN BUILDING

Start-up operations: 2008
 Usable area: 4 131 m²
 Lab space: 1 867 m²
 Offices: 1 615 m²
 Seminar area: 276 m²

SECOND EXTENSION BUILDING

Start-up operations: 2015
 Usable area: 3 050 m²
 Lab space: 1 171 m²
 Offices: 881 m²
 Clean rooms: 402 m²

RENTAL AREA AT BIO CITY LEIPZIG

Start-up operations: 2006
 Clean rooms: 334 m²



**LOCATIONS &
DEPARTMENTS**

LEIPZIG, SAXONY, GERMANY

HEADQUARTER

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 (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 1 200 m².

MANAGEMENT

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LEIPZIG, SAXONY. GERMANY

MAIN DEPARTMENT OF GMP CELL AND GENE THERAPY



The Main Department of GMP Cell and Gene Therapy operates Fraunhofer IZI's 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.

CORE COMPETENCIES

- Quality assurance
- 1 000 m² clean rooms
- ATMPs
- GMP process and method transfer
- Manufacturing authorization according to §13 AMG
- Investigator Medicinal Product Dossier (IMPD)
- Good Manufacturing Practice (GMP)
- Manufacturing and quality control of ATMPs

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LEIPZIG, SAXONY, GERMANY

DEPARTMENT OF GMP PROCESS DEVELOPMENT / ATMP DESIGN



The Department of GMP Process Development / ATMP Design is responsible for transferring manufacturing processes from the lab into a clinical setting. In order to obtain official manufacturing licenses for the production of clinical test samples, either GMP-compliant processes are developed from scratch or existing processes adapted and optimized.

The department focuses primarily on cell- and gene-based drugs, known as Advanced Therapy Medicinal Products (ATMPs). These include antigen-specific T cells, CAR-T cells, CAR-NK cells, dendritic cells, mesenchymal stem cells (MSC), induced pluripotent stem cells (iPS) and tissue engineering products.

Furthermore, upstream and downstream processes are being developed for biomolecules in single-use reactors with a volume of up to 200 liters.

The development of GMP-compliant manufacturing protocols is closely associated here with the definition of respective quality controls.

In the development unit, process adjustments can be tested and optimized flexibly and cost-efficiently. The impact of new devices, media, seed densities and freezing protocols on the GMP process is also investigated here.

This then enables new processes to be implemented and validated in the institute's GMP clean rooms..

CORE COMPETENCIES

- GMP process development and transfer for ATMP manufacturing
- mRNA technology
- Specialist expertise in hematology / oncology
- Process optimization and automation
- Good Manufacturing Practice (GMP) evaluation for ATMP manufacturing
- Quality assurance
- GMP-compliant equipment and processes
- Clinical trial planning
- CAR-NK cells and NK cell technologies
- Biomaterials research
- Non-clinical developments (in vitro and in vivo)
- Preparing GMP documents (SOPs, batch records, quality control records...)
- GMP process development for biopharmaceuticals
- GMP certification
- Manufacturing authorization for therapeutic antibodies pursuant to Section 13 (1) of the German Medicinal Products Act (AMG)

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DEPARTMENT OF PRECLINICAL DEVELOPMENT AND VALIDATION



The main goal of the Department of Preclinical Development and Validation 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 Fraunhofer IZI departments) can be performed under GLP.

CORE COMPETENCIES

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

THE DEPARTMENT COVERS THE FOLLOWING TOPICS

- 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.
- 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).
- 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.
- Developing human monoclonal antibodies to be directed against new therapeutic tumor targets (triple-negative breast cancer) and to be used as passive vaccines against pathogenic viruses (SARS-CoV-2) besides their further development as drug candidates.

CONTACT

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PRECLINICAL MODELS UNIT

The Preclinical Model 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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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 particularly in the context of developing and testing novel implants as well as for the medical indications triple-negative breast cancer and chronic inflammatory bowel disease. Multi-omics strategies (especially LC-MS based proteomics) are applied for biomarker detection as well as for the study of disease- or agent-induced effects.

Prof. Dr. Stefan Kalkhof also holds a research professorship position for instrumental bioanalytics at the Coburg University for Applied Science. This synergy enables the application of additional spectroscopic and mass spectrometric approaches e.g. for the direct chemical analysis of implants.

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CELL LINE DEVELOPMENT UNIT

The Cell Line Development Unit is focused on the detection strategies of biomarkers and molecules based on monoclonal antibodies produced in house. Building on our experience in the field of human and veterinary diagnostics as well as in the area of food allergy analytics, we are working with the user to develop immunology singleplex and multiplex assays. With regard to cell line development for biopharmaceuticals, we draw not only on automated cloning and selection, but also on the label-free detection of biomolecules in real time by means of surface plasmon resonance spectroscopy (SPR). This enables the product to be quantified and quality-controlled throughout the entire development process.

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VETERINARY PATHOLOGY UNIT

The Veterinary Pathology Unit carries out histopathological and toxicopathological examinations as part of GLP studies investigating the safety and efficacy of drug candidates. In accordance with the regulatory requirements concerning test candidates for new drugs or medical devices, tests for local effects after application and / or toxicity testing, for instance, are carried out in order to ensure that the test candidates are not expected to pose any health risks.

The unit's portfolio covers the planning, drafting, validation, implementation and evaluation of histological test procedures. All work processes, from sampling to processing through to the appropriate histochemical and IHC staining of tissue sections, are carried out in line with relevant SOPs. Various sample systems generated by the group such as paraffin-embedded and cryo-preserved tissue samples, stained tissue sections and also remaining samples are collected in a biobank and archived in compliance with GLP following study completion. The digitalization of tissue sections completes the GLP trial portfolio.

CONTACT

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LEIPZIG, SAXONY, GERMANY

DEPARTMENT OF VACCINES AND INFECTION MODELS



Procedures to stimulate or suppress the immune system are developed in the Department of Vaccines and Infection Models. 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. An S3 laboratory facilitates work with highly infectious pathogens. In-vivo and in-vitro model systems are also generated and used to develop diagnostic and therapeutic agents.

CORE COMPETENCIES

- Antimicrobial peptides
- Vaccine development
- Immunological models
- Inactivation of pathogens / antibody development
- Working with highly infectious pathogens

CONTACT

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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, SARS-CoV-2 or influenza. Besides this, strategies are being developed to combat ectoparasites.

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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 trials 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.

CONTACT

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INFLAMMATION MODELS AND IMMUNODIAGNOSTICS UNIT

This unit holds a broad spectrum of in vivo models for preclinical proof-of-concept studies. We focus on autoimmune induced joint diseases (e.g. Rheumatoid Arthritis), airway diseases (e.g. bronchial asthma, allergic rhinitis) and chronic kidney diseases. Other main topics are tumor models and humanized in vivo models. In addition, the group specializes in routinely developing new research models as well as in diverse methods of analysis to investigate the in vivo models

CONTACT

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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 antibiois.

CONTACT

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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.

CONTACT

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LEIPZIG, SAXONY, GERMANY

DEPARTMENT OF DIAGNOSTICS



The Department of Diagnostics offers a value chain that covers the identification and testing of new biomarkers, the bioinformatic analysis of complex transcriptomic and genomic data ("Big Data") as well as the development of prototypes for in vitro diagnostics and point-of-care platforms. Furthermore, it offers a broad range of analytical methods.

In the department's RIBOLUTION Biomarker Center new biomarkers are being systematically identified and validated using state-of-the-art techniques such as next-generation sequencing (NGS) and microarray analysis. A particular focus is on non-coding RNAs, which show high, so far mostly underestimated, biomarker potential. An experienced bioinformatics group provides efficient processing and (statistical) analysis of molecular biological data, particularly of NGS data obtained from large clinical cohorts. Competencies in study and data management enable our scientists to plan and conduct such cohorts. A quality management system has been implemented and certified according to ISO 9001:2015 with an eye to these processes.

A main focus of the department is to develop molecular and immunodiagnostic tests in the medical and food sector. This includes PCR and NGS analyses, lab-on-a-chip systems as well as peptide selection and epitope mapping technologies. Diagnostic needs are addressed e.g. for cancer, cardiological diseases and food allergies as well as pathogen tests for

infectious diseases. Moreover, the department has a wide range of additional analytical methods at its disposal and develops novel biointeractive molecules on structural DNA-based scaffolds. New imaging procedures support the analysis of cell biological processes.

CORE COMPETENCIES

- Transcriptome and immunome analyses
- Next-generation-diagnostics
- Bioinformatics
- Nanotechnology
- Lab-on-chip
- Biomarker identification
- Tumor models
- Quality assurance according to DIN EN ISO 9001:2015
- Experimental imaging and image analysis
- Tumor tissue-specific peptides
- Epitope mapping in patient sera

CONTACT

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CARDIOMICS UNIT

The group uses state-of-the-art OMICS technology platforms to research cardio-surgical locally and systemically relevant infectious diseases. The focus of scientific interest is in particular the crystallization of pathogen-specific virulence factors and their influence on the clinical outcome after implantation of a medically necessary device or implantation of biological or mechanical heart valves as well as their translation into clinical routine. Based on improved diagnostics, alternative treatment methods are evaluated and new interventional procedures taken to clinical maturity. In particular, the working group examines the relationship between infectious diseases and molecular regulatory mechanisms. 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 research group primarily develops diagnostic procedures for determining the effect of factor X inhibitors or coagulation diagnostics in the final section of the plasmatic and thrombocytic coagulation cascade.

CONTACT

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LIGAND DEVELOPMENT UNIT

The unit is focused on immunological and oncological issues. A proprietary, statistical phage display method is used for mapping antibody epitopes (in sera, e.g. allergy or infection diagnostics) and also for detecting therapeutic or cell-specific ligands (e.g. tumor targeting). A huge amount of work is also being done on primary cell, tissue and organoid models for developing and testing new ligands. To this end, the unit has access to state-of-the-art equipment (FACS, imaging) as well as patented methods for iPS cells and surface modifications for the cell culture. Cooperations are giving rise to new insights into immunological diseases, serological evidence, and also image evaluation methods using cells or peptide microarrays. One successful spin-off and a second in planning highlight the pertinence of ongoing research projects.

CONTACT

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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.

CONTACT

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IMAGE ANALYSIS OF CELL FUNCTION UNIT

This unit develops methods for tailored image analysis as well as algorithms for microscopy-based quantification of physiological and pathological processes. The direct and collegial collaboration with life scientists at the institute as well as with external partners can ensure that the tools developed are targeted at meeting the requirements.

The pursuit of two main goals defines the unit's strategy. On the one hand, to implement a high degree of automation for image analyses that can in principle also be solved manually (cell counting, intensity measurement, morphology description, etc.) and on the other hand to create methods for questions without established solutions (e.g. AI annotation of prostate tumors in histological specimens).

Furthermore, the aim of the working group is to support the research of basic biological relationships and to test new therapeutic methods by analyzing cells and tissue without altering or destroying them.

CONTACT

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MICRODIAGNOSTICS UNIT

The unit develops molecular diagnostic test systems for the food and medical-clinical area. A major focus is on the use of extracellular vesicles for the early diagnosis of Alzheimer's or cancer, the development of rapid tests for infectious agents and bioanalytical sample preparation. Novel lab-on-a-chip diagnostic platforms, e.g. for the detection of sexually transmitted pathogens in home test format, are being developed with customers. Another focus is on airway analysis using ion mobility spectrometry. Hot embossing technology is available in-house for microfluidics development.

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DNA NANODEVICES UNIT

The DNA Nanodevices group focuses on developing and implementing nanometer-scale tools for biomedical research. DNA molecules and their characteristics are used to arrange and structure biomaterials on the nanometer scale. This type of technology is applied to develop molecular components for diagnostic assays, in addition to being used to discover and develop new compounds to inhibit infections from viruses or bacteria. To this end, the unit investigates the biochemical and biophysical characteristics of specific DNA molecules and composite materials to quantify their specific interactions and mechanisms of action with biological organisms.

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NEXT-GENERATION DIAGNOSTICS UNIT

The focus lies on identifying and validating new diagnostic and prognostic RNA biomarkers for various diseases. A wide range of state-of-the-art molecular methods (e.g. next generation sequencing) for the GLP-oriented screening and validation process are applied. These methods are continuously improved according to technological developments.

Increasing focus is being placed on companion diagnostics as well as on characterizing cells for use in cell-based therapies, which represents an important step towards personalized healthcare.

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BIOINFORMATICS UNIT

The Bioinformatics Unit develops and establishes computer-aided methods for identifying and verifying RNA biomarkers for the precise diagnosis and prognosis of diseases as well as for the detection of novel therapeutic targets. The aim here is to characterize RNA molecules as biomarkers and therapeutic targets by using transcriptome-wide approaches, and to establish them in clinical practice.

A high number of RNA molecules are not translated into proteins. These so-called non-protein-coding RNAs (ncRNAs) perform fine-regulatory tasks in gene regulation and are therefore suitable as markers or therapeutic targets for individual disease patterns and progression. RNA-based approaches are becoming increasingly significant in oncology and immuno-oncology due to their ability to quantify the activity of genes, i.e. the product of genome and epigenome, in cells at a specific point in time.

The unit develops strategies for the efficient processing and statistical analysis of molecular biological data gained from extensive clinical cohorts based on next generation sequencing (NGS), microarrays, as well as DNA, RNA and epigenetic analytics. Machine and statistical learning behaviors will be implemented and used here in order to analyze disease-relevant molecular mechanisms as well as to

characterize and validate RNA biomarkers and RNA-based targets (incl. ncRNAs) for oncology and immuno-oncology.

All processes are implemented according to the regulatory requirements, ensuring the developed prototypes can be successfully transferred into medical applications (e.g. IVDs). The unit works in line with a certified quality management system (ISO 9001:2015).

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DEPARTMENT OF EXTRACORPOREAL THERAPY SYSTEMS



The Department of Extracorporeal Therapy Systems focuses on the development and evaluation of extracorporeal (outside the body), organsupporting technologies with a particular emphasis on supporting the immune system. It offers 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, the department offers self-developed unique analytic and diagnostic devices including an ex situ intestinal model, a cell sensor and novel protein assays.

CORE COMPETENCIES

- Cellular biosensors
- Medical devices for blood purification
- Dialysis procedure
- Organ-supporting technologies

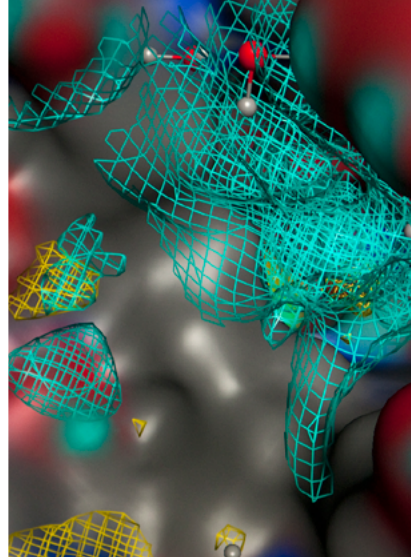
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HALLE (SAALE), SAXONY-ANHALT, GERMANY

DEPARTMENT OF DRUG DESIGN AND TARGET VALIDATION



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.

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.

CORE COMPETENCIES

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

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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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SACHSEN-ANHALT



EUROPÄISCHE UNION
EFRE
Europäischer Fonds für
regionale Entwicklung

ASTACIN PROTEASES UNIT

The human genome contains information for about 600 proteolytically active enzymes involved in a variety of different regulatory processes. A disturbed or deregulated function of these proteinases therefore often leads to the development of diseases.

An interesting family of proteinases are the astacins, which in the human organism comprise the bone morphogenetic protein 1 (BMP-1), the meprins α and β and ovastacin. Furthermore, astacin proteases of other organisms, e.g. parasitic pathogens, are also potential drug targets. In recent years, meprins in particular have moved into the focus of drug research and represent promising targets for the treatment of kidney disease, fibrosis and cancer.

Based on the recently gained knowledge on inhibitors of meprins, the group is working on the design and further development of meprin inhibitors. In addition, the first inhibitors of ovastacin are being developed, which is also an innovative and interesting drug target for the treatment of infertility. In addition to these human proteinases, astacins from parasitic nematodes will also be addressed in order to develop novel drugs for the treatment of worm diseases.

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POTSDAM-GOLM, BRANDENBURG, GERMANY

BRANCH BIOANALYTICS AND BIOPROCESSES

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 (CCryo), which serves as a resource for developing production processes for novel, industrial bioproducts.

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DEPARTMENT OF BIOSYSTEM INTEGRATION AND PROCESS AUTOMATION



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

The department 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.

CORE COMPETENCIES

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

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LABORATORY AND PROCESS AUTOMATION UNIT

The working group abstracts complex laboratory processes from biotechnology, isolates and transfers the processes and develops automation solutions from them.

In addition to manufacturing and production processes, the focus is on diagnostic developments with an immunological and molecular biological basis and a particular interest in rapid isothermal processes and their detection.

The aim of all developments is to increase the efficiency as well as the quantity and quality of the processes to be automated.

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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. We focus on applications for point-of-care testing, however applications in a laboratory environment are also included. The unit covers a broad range of microscopy techniques 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 and innovative biomimetic materials and coatings. Homogeneous assays with an affordable electrochemical read-out system are one focus, but also innovations of mature assay technologies: Our hydrophilic surface coating for plastic disposables TruContact® minimizes antibody and sample consumption as well as unspecific protein binding in ELISA. "Smart" dry reagents simplify the shipping and storage of diagnostic kits due to their enhanced shelf life and customer-specific added functionalities such as enhanced adhesion and optical transparency. Biomimetic electrochemical sensors, functionalized with artificial binding molecules (MIPs, "plastic antibodies"), offer new analytical options if antibodies are not available or desired. A new research focus is biomimetic materials for 3D printing.

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IVD PLATFORM / POC TECHNOLOGIES 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 body fluids.

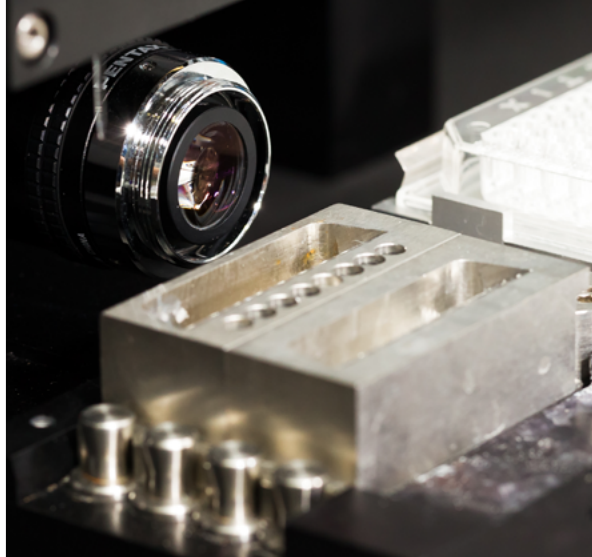
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POTSDAM-GOLM, BRANDENBURG,
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DEPARTMENT OF MOLECULAR AND CELLULAR BIOANALYTICS



The department deals to develop 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 department develops point-of-care tests, e.g. for drug and serum screening, and likewise 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.

CORE COMPETENCIES

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

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MICROFLUIDIC CELL PROCESSING AND CELL ANALYTICS UNIT

The focus of the research group lies in developing microfluidic devices for high-precision stem- and immune cell handling, as well as processing other delicate biological samples. Combined with automated image analysis, individual target cells in heterogeneous cell samples can be identified on the basis of their microscopic image and selectively processed or separated. Another focus of the research group is the development of high-performance test systems for analyzing the blood compatibility of cardiovascular medical devices under highly-controlled flow conditions.

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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, physico-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 and their application within the scope of antibiotic resistances. NGS is applied to analyze genes and RNA species from pathogens.

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MICROSYSTEMS FOR IN VITRO CELL MODELS UNIT

The Microsystems for In Vitro Cell Models Unit develops customer-specific, efficient methods and prototypes for the cultivation, characterization and processing of demanding cell samples. The design and implementation of innovative concepts are based on the group's comprehensive expertise in microreactors, microfluidics, sensor technology and functional polymer coatings, and on its know-how in cell biology, toxicology and bioanalytics. The interdisciplinary orientation of the research unit enables a well-founded and targeted advice as well as an efficient execution of the customer's specific needs. Activities focus on (i) developing in vitro test methods for assessing the toxicity of drugs and chemicals based on organ-on-chip systems and relevant cell models, as well as (ii) establishing intelligent polymer coatings which allow the behavior of adherent cells on technical surfaces to be controlled.

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MICROARRAY AND BIOSENSOR TECHNOLOGY UNIT

Currently, the request for fast information generation is rapidly increasing, and this also applies to analytical questions about “WHAT” or “HOW MUCH” to draw conclusions about one's own behavior.

The “interface problem” is a major obstacle wherever natural structures meet technical systems.

Another is the challenge to draw as much analytical information as possible from as little and as native material as possible.

The solution lies in the modification of the respective surfaces. Through defined (bio)chemical functionalization, e.g. by branched linkers or the application of thin films using biopolymer-based membranes or switchable hydrogel layers, surfaces with new properties or so-called intelligent surfaces are created. The technological implementation takes place both on geometric materials such as fibers and on planar carriers such as plates or chips. The treatable surfaces themselves vary from glasses and wafer materials to natural fibers and plastics.

The result is independent sensor elements (e.g. test strip-based PoNd) or biosensor-based analytic tools (e.g. cell and peptide chips), for which various questions from the fields of environmental analysis, food monitoring, herd management, process control or diagnostics can be used on site and enable immediate data evaluation and transmission.

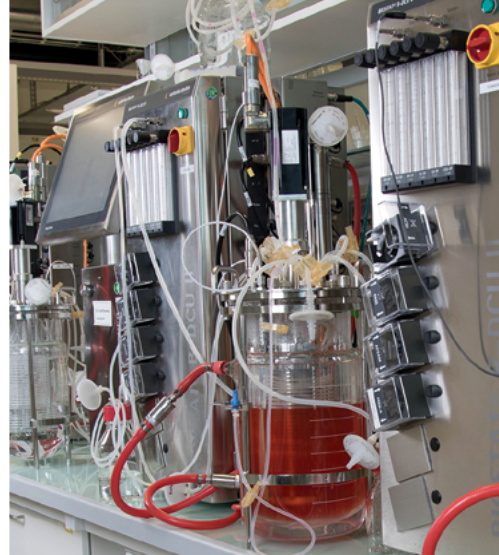
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POTSDAM-GOLM, BRANDENBURG, GERMANY

DEPARTMENT OF CELL-FREE AND CELL-BASED BIOPRODUCTION



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 in the health care sector. Active agents and analytes, biomolecules such as enzymes, antibodies and aptamers often are key molecules 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. By using the subcellular components of the organisms required for synthesis in suitable reaction environments it is possible 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 a focus.

CORE COMPETENCIES

- 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

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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 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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EUKARYOTIC LYSATES UNIT

The unit develops cultivation systems of eukaryotic cell lines for the production of translational lysates for protein synthesis. In this respect, the testing of cell lines for their in vitro expression capabilities is of the highest interest. Furthermore, the unit continues to develop and optimize cell-free eukaryotic translation systems and investigates the influence of fermentation, cell disruption, and transcriptional and translational components on the productivity of the lysates. Based on this, the synthesis of proteins can be carried out in cell-free systems under the optimal conditions for the respective protein. The optimal synthesis conditions are protein-specific and are determined in evaluation studies. On request, protein syntheses can also be carried out under GLP conditions.

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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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POTSDAM-GOLM, BRANDENBURG, GERMANY

EXTREMOPHILE RESEARCH & BIOBANK CCCRYO



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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ERFURT, THURINGIA, GERMANY

PROJECT CENTER MICROELECTRONIC AND OPTICAL SYSTEMS FOR BIOMEDICINE

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.

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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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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 and quality control processes and spaces with regard to drug manufacturing. It regulates, among other things, the requirements concerning hygiene, human resources, facilities, equipment, documentation and controls.

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

BIOPHARMACEUTICALS

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 production of biopharmaceuticals 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. Besides the clean room facility, the institute operates a process development unit where relevant manufacturing processes are designed and upscaled and where respective quality control tests are established and checked for suitability. Alongside projects involving recombinant proteins, virus-associated projects can also be conducted here up to biosafety level 2.

The manufacturing team's portfolio includes transferring biopharmaceutical candidates from preclinical research into clinical development, drafting user-specific processes and manufacturing.

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 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).

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WHY ARE GMP AND GLP 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 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.

IMAGING AND IMAGE ANALYSIS



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)

- 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)

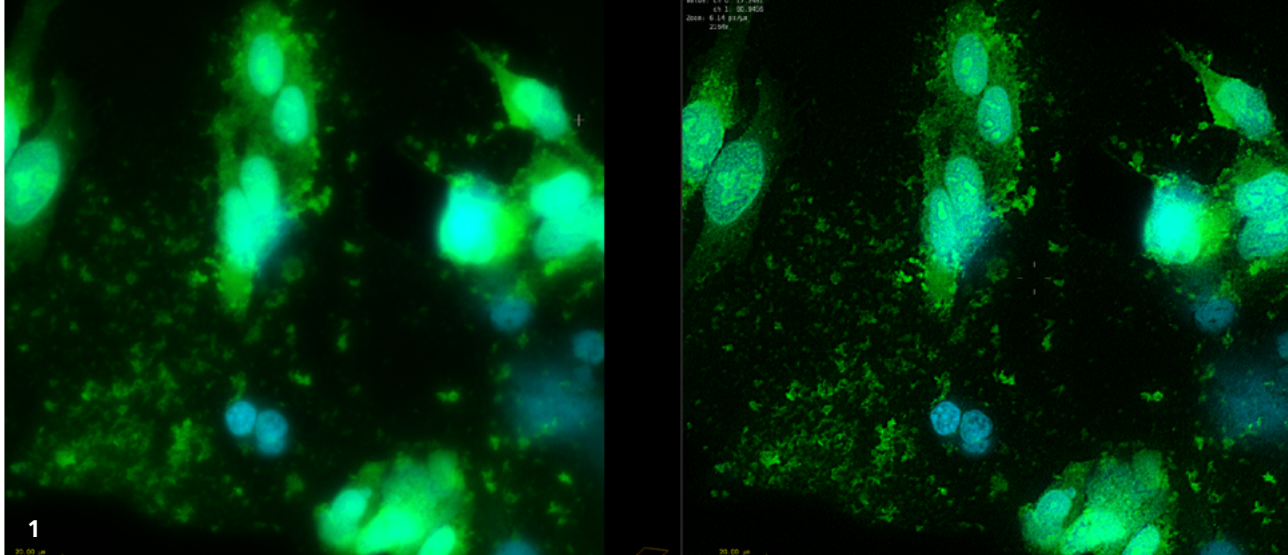
- Depiction of dense (bone, cartilage) and contrast-enhanced (soft tissue) structures
- 3D data sets can be used for conformal radiation treatment planning

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



IN VITRO / EX VIVO IMAGING

Clearing tissue samples

- 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

- 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

CONTACT

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1 *Improved epifluorescence microscopy images (elimination of photon noise and blurring caused by diffraction) by means of deconvolution capture a much greater level of detail.*

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



The Biomarker Center received a new seal of quality in June 2020. Following successful certification by TÜV Rheinland, a quality management system was established in accordance with ISO 9001:2015 under the direction of Professor Friedemann Horn, Dr Conny Blumert (Next-Generation Diagnostics Unit) and Dr Kristin Reiche (Bioinformatics Unit).

In the Biomarker Center, new diagnostic and prognostic RNA biomarkers are systematically and comprehensively identified and validated using cutting-edge technologies such as next generation sequencing (NGS). Expertise in managing studies and data is essential when it comes to planning and arranging clinical cohorts as well as handling clinical and experimental data. The biomarker screening process is also being optimized and perfected with the aid of technical innovations. Since June 2020, the procedures involved here have been governed by a certified quality management system (ISO 9001:2015).

The TÜV certificate specifically covers: “Research and commissioned work in the field of molecular diagnostic analytics and the related bioinformatic evaluation, with emphasis on personalized medicine as well as optimizing and developing modern processes and applications for molecular diagnostics including next generation sequencing”. The appraised quality management system ensures that internal operations, service quality, and partner and customer relationships are all overseen by a quantifiable system at the Biomarker Center. This means that processes are mapped precisely, their efficiency increased, and internal errors

reduced. Process validation is another important aspect at the Biomarker Center. If a process is documented, evidence can always be provided to show that it fulfills the demands placed on a particular service and that it delivers reliable, transparent results. This enables competitive research and development projects to be driven forward together with clinical partners and interested research partners.

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S3 SAFETY LABORATORY



Fraunhofer IZI operates a safety level 3 laboratory, making it possible to handle research and development projects under biosafety level 3 conditions and to investigate highly pathogenic agents. Genetic engineering work can also be undertaken. Adjacent premises for keeping animals permit the development of and work with infection models for corresponding types of pathogen.

Safety precautions taken in the S3 laboratory include an independent ventilation system with separate filters (H14 class HEPA filters) for all rooms incl. autoclave. High-efficiency particulate air filters eliminate 99.995 percent of all particles measuring between 0.1 and 0.3 micrometers. The ventilation system guarantees eight air changes per hour with an air flow volume of up to 1500m³/h air throughput.

Airlocks and pressure differences between areas prevent infectious particles from escaping into the air. Every room can also be aerated and ventilated separately to eliminate contamination.

Staff safety is ensured through specific training measures, special safety clothing and protective hoods with integrated air filter systems.

FACILITIES

The S3 laboratory is equipped with a safety cabinet, various centrifuges, an inverted microscope with phase contrast, a refrigerator, a -80°C ultra-low freezer, an incubator and a thermal cycler for cellular and molecular biology work.

Standard activities include using cell cultures for virus propagation, using assays to determine viral concentration (TCID₅₀, plaque assay), and virus inactivation. Neutralization assays can also be carried out.

The laboratory is currently being used to examine viruses transferred by arthropods such as the dengue or West Nile viruses alongside SARS-CoV-2. Other pathogens that fall under biosafety level 3 can be added as required.

ACHIEVEMENTS AND CONTRACT RESEARCH

- Testing and developing drugs in vitro and in vivo
- Testing and developing vaccines
- Immunology studies (e.g. analyzing protective antibodies from patients), also in cooperation with hospitals
- Material testing (e.g. antiviral coatings)
- Testing disinfectants
- Virus stability testing
- Establishing infection models on lab-on-a-chip technologies

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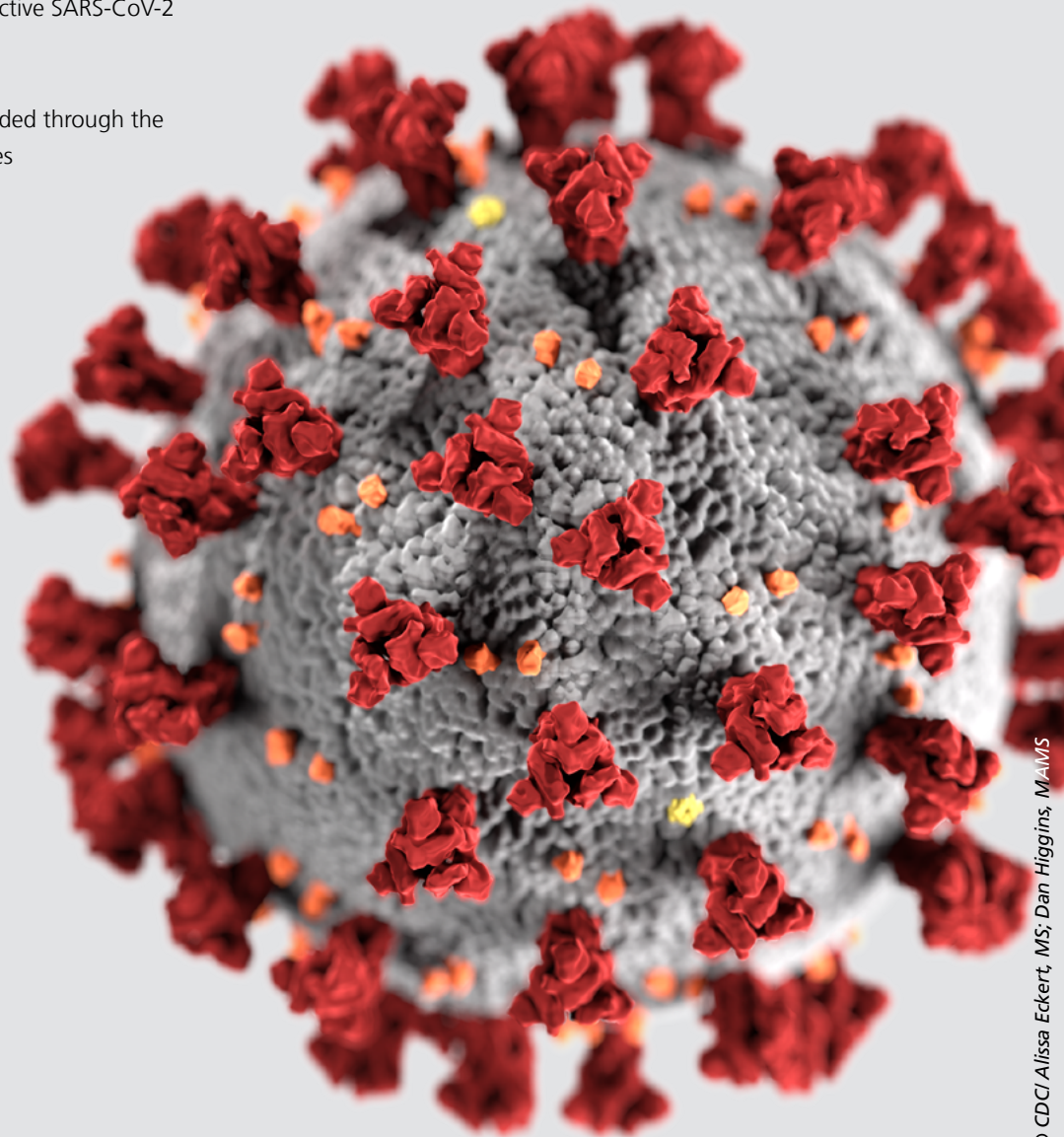
**SELECTED
PROJECTS**

CORONA PANDEMIC

United against corona – Fraunhofer experts are on the front line in the fight against Covid-19, helping the economy and society to overcome the immediate effects and future consequences of the pandemic.

Fraunhofer IZI is involved in various projects aimed at investigating, developing and optimizing solutions for diagnostic, preventive and therapeutic procedures. Infection models and work in the S3 safety laboratory (see page 54), where research can be conducted using the active SARS-CoV-2 virus, form a focus here.

The majority of projects are largely funded through the Fraunhofer-Gesellschaft's own resources





INFECTION PREVENTION THROUGH SMEAR-FREE ON-SITE TESTING FOR SARS-COV-2

The project aims to provide a procedure as quickly as possible that allows simple on-site testing for a possible infection.

For precise interventions, the identification of a viral infection should be done at a very early stage, preferably by persons without symptoms. This is crucial for the management of patients and infected nursing and clinical staff.

For a test for SARS-CoV-2, smear samples are taken by a swab of the nasal/pharyngeal mucosa. A correctly performed, deep smear can be unpleasant to painful. Sources of error here are incorrect sample collection and the wrong time for the smear, as the throat is often only slightly affected in later phases of the disease. The actual examination of the sample material is currently carried out in central laboratories and provides the results the next day at best.

The goal of the project is an apparatus-free respiratory gas analysis for preventive monitoring of the health status, especially for persons in systemically relevant professions. For self-protection reasons, medical professionals are obliged to wear a mask. It is therefore logical to integrate the sensor into the face mask. For this purpose, the mask is equipped with a flexible test matrix, which is a tool for both sample collection and analysis. The advantage of a sensory breath analysis for virus detection is that sampling is non-invasive,

unlimited in terms of volume, does not require clinical personnel and does not represent a significant burden for the test person. The test result would be immediately visible, even if the actual symptoms of an infection are not yet noticeable. For a comprehensive monitoring in case of a second corona wave, there would be no higher psychological and physical stress for medical personnel in particular due to constant smear tests.

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1 *Model of a breathing mask with integrated sensor.*



CELL-FREE PROTEIN SYNTHESIS AS RAPID RESPONSE TO COVID-19

A feasibility study evaluating the qualification of cell-free protein synthesis as a platform technology for the rapid synthesis of viral proteins, including potential mutations, is in the focus of this project. The production of viral proteins in conventional cell-based processes is often limited by the negative effects of these proteins on the viability of the cells. The results are low protein yields and reduced protein quality. A further obstacle in the production of viral proteins is the high safety level in the expression of viral proteins in cell-based systems.

Cell-free protein synthesis offers a platform technology for the synthesis and characterization of difficult-to-produce proteins, as the open system can be adapted directly to the individual protein. High safety levels are not necessary due to the use of a cell lysate. Thus, in vitro protein synthesis opens up the possibility to investigate proteins of viral origin that are currently not or only inefficiently producible. The availability of a fast and efficient method to provide such viral proteins for the development of diagnostics and therapies is of crucial importance for the health care system. In the course of this start-up funding, viral proteins expressed by SARS-CoV-2 are to be produced by cell-free protein synthesis within 60-90 minutes without generating genetically modified organisms. Not only already well characterized proteins like the spike protein, but also various other viral

proteins of the ORFs 1-10 are planned to be produced in cell-free synthesis. These proteins can be functionally characterized and made available to various other partners and the Fraunhofer-Gesellschaft as "services" for serological screening and antibody tests. Viroporin proteins in particular, such as the coronavirus envelope protein, are subjected to detailed functional analysis at the Fraunhofer IZI-BB.

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BEAT-COVID – BUILT-UP EXISTING AND ADVANCED THERAPY STRATEGIES AGAINST COVID-19

The corona pandemic highlights the need to prepare against emerging pandemic-spreading infections by establishing platform technologies for the rapid development of new antiviral strategies. Advanced Therapy Medicinal Products (ATMPs), especially those based on genes, are particularly interesting and are promising therapies for infectious diseases. As a platform technology, they can be used not only in the context of the current pandemic against SARS-CoV-2, but also against future, currently unknown pathogens in a very targeted manner against respective virus-specific targets. The further development of highly specific inhalable antibodies for the regulation of the excessive immune response in lung failure also represents promising therapeutic approaches.

The project consortium focuses on novel therapies for the treatment of COVID-19 in particular and infectious diseases in general. The team will develop novel therapeutic strategies to inhibit the entry of SARS-CoV-2 into respiratory epithelial cells. These could be used to reduce viral replication to prevent COVID-19 disease. Another project goal is the development of a therapy to inhibit the excessive immune response of COVID-19 by inhalation of anti-inflammatory antibodies. Fraunhofer IZI contributes to the project with its long-standing expertise in terms of production and preclinical evaluation of ATMPs, biomolecules and vaccines. The departments Preclinical Development and Validation, GMP Process Development / ATMP Design as well as Vaccines and Infection Models are involved in the project.

PARTNERS

- Fraunhofer Institute for Toxicology and Experimental Medicine ITEM (Coordination) | www.item.fraunhofer.de/en
- Fraunhofer Translational Center for Regenerative Therapies TLZ-RT at the Fraunhofer Institute for Silicate Research ISC | www.isc.fraunhofer.de/en
- Fraunhofer Institute for Applied Polymer Research IAP | www.iap.fraunhofer.de/en
- Fraunhofer Institute for Reliability and Microintegration IZM | www.izm.fraunhofer.de/en

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C19 LUNG CHIP – DRUG REPURPOSING USING A COVID-19 INFECTION MODEL IN AN IMMUNOCOMPETENT LUNG-ON-CHIP PLATFORM

Organ-on-chip platforms integrate complex tissues in a micro-physiological environment with the aim of simulating human biology outside the human body and even integrating aspects of the human immune system. The C19 lung chip project combines the skills and know-how of the Fraunhofer Institute for Interface Engineering and Biotechnology IGB in using organ-on-chip platforms for pharmaceutical studies with the expertise of the Fraunhofer Institute for Cell Therapy and Immunology IZI in infection models as well as its existing experience with the SARS-CoV-2 virus. The Immunology department has the only safety level 3 laboratory within the Fraunhofer community. This constitutes a precondition for working with highly pathogenic viruses, such as the SARS-CoV-2 virus.

At present, there are hopes of finding a treatment for COVID-19 infections through drug repurposing, i.e. the use (of combinations) of approved drugs. A number of possible candidate drugs have already been identified in various studies and there already are (more or less substantiated) reports regarding successful treatment for some of these.

In the framework of the C19 lung chip project, the scientists want to carry out non-clinical studies with the help of a lung model system. This helps to significantly speed up the first explorations as to the effectiveness of certain substances in the fight against SARS-CoV-2, compared with conventional methods, such as the use of animal models. Furthermore, the organ-on-chip technology is also supported by the fact that the current exceptional situation and the extreme strain on the healthcare systems make the execution of extensive and protracted clinical studies for a large number of possible

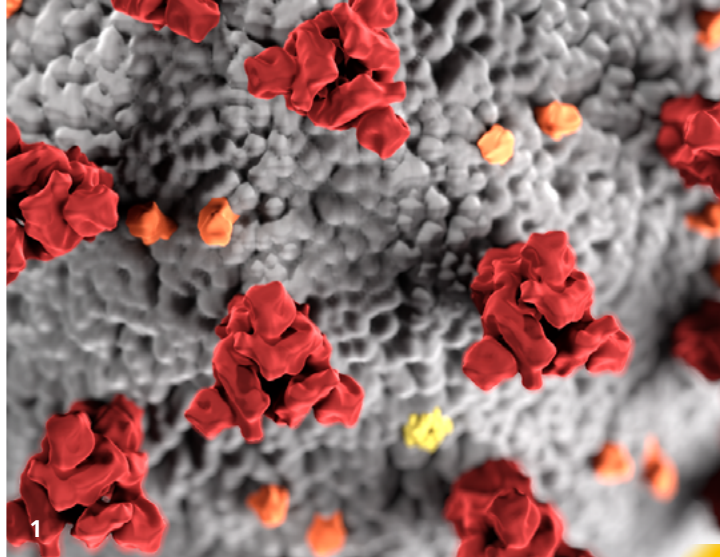
therapeutics very difficult. Therefore, methods for the fast, resource-saving pre-clinical validation of possible candidate substances are very helpful. Against this backdrop, the C19 lung chip project initially aims to establish a COVID 19 lung infection model which simulates the pathogenesis of COVID-19. As a second step, this model is then to be used to test the effectiveness of up to 40 different substances or substance combinations.

PARTNERS

- Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB (project lead) | www.igb.fraunhofer.de/en.html
- Fraunhofer Institute for Molecular Biology and Applied Ecology IME, Division Molecular Biotechnology | www.ime.fraunhofer.de/en

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CORONASENSE – COVID-19 PEPTIDE BINDING ANALYSIS FOR DIAGNOSTICS AND TREATMENT

Knowledge of the sites at which the virus binds to its host cell and understanding its binding behaviour are of fundamental importance for designing active ingredients that can stop the binding process and also for the development of diagnostic tests based on such binding. Since SARS-CoV-2 has many spike proteins on its surface, bindings can appear at several binding peptides if the density of the DNA lever is suitably adjusted. Compared with the affinity of the first binding, every further binding leads to a significant increase in affinity. This has already been proven in influenza viruses by the Bioanalytics and Bioprocesses Branch of the Fraunhofer Institute for Cell Therapy and Immunology.

Accordingly, multivalent binding partners provide a promising option for the inhibition of viruses on the host cell. The binding kinetics of these multi-valent bonds can be established with the help of the SwitchSense technology. Virus-like particles or surface-modified particles with bound spike proteins are to be used for these measurements. Moreover, the size of the viruses can also be determined using the SwitchSense technology, which provides a further measurement parameter for characterising a virus sample in terms of its homogeneity and a further characteristic for differentiating various viruses.

In the CoronaSense project, a nano-structure with a nucleic acid scaffold and virus-binding peptide moieties (patent: WO2018215660A1) is to be exploited by the Fraunhofer IZI DNA Nanodevices Unit.

PARTNERS

- Branch of Bioanalytics and Bioprocesses at the Fraunhofer Institute for Cell Therapy and Immunology IZI | www.izi-bb.fraunhofer.de/en
- Dynamic Biosensors GmbH | www.dynamic-biosensors.com
- PSL Peptide Specialty Laboratories GmbH | www.peptid.de/en

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COROVACC – DEVELOPMENT OF A SARS-COV-2-SPECIFIC VACCINE BASED ON HERPES VIRUSES

Over recent decades, vaccines, which are by far the most effective preventative measure against infectious diseases, have contributed decisively to the reduction of illnesses and even the eradication of pathogens. Vaccines based on attenuated viruses, in particular, are highly effective since they induce both aspects of the immune response – on the one hand, the humoral aspect through the production of pathogen-specific antibodies and, on the other hand, the cellular aspects through the T cell-mediated immune response.

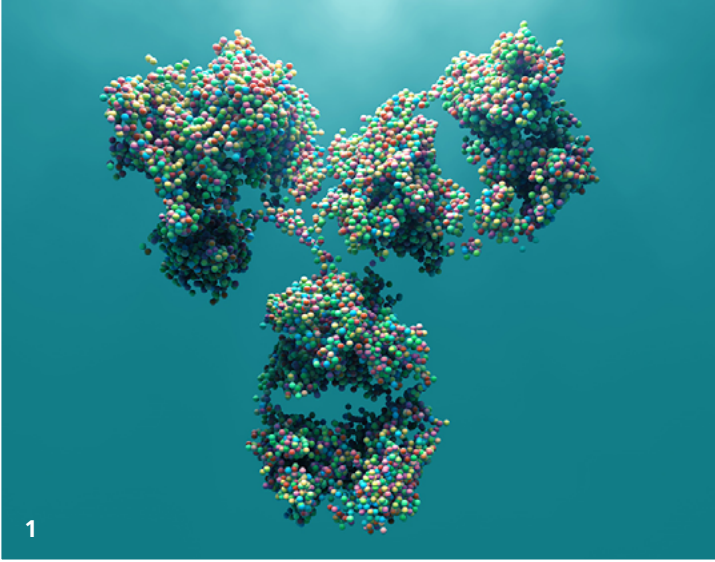
The Corona pandemic is highlighting the fundamental importance of the fast development of effective vaccines for new pathogens. In the framework of the CoroVacc project, scientists from the Fraunhofer Institute for Interface Engineering and Biotechnology IGB and from the Fraunhofer Institute for Cell Therapy and Immunology IZI are working to develop a Sars-CoV-2-specific vaccine virus based on an established platform vector (herpes virus derivative). The developed platform technology can quickly adapt the herpes virus vectors on a modular basis. As a result, new infectious agents emerging in future can be quickly addressed. The high genomic capacity of the viral vector (permitting the use of a combination of several pathogens or antigens as a vaccine) is one of its special features.

PARTNER

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COVER-AB – HUMAN ANTIBODIES AGAINST SARS-COV-2 FOR COVID-19 PREVENTION AND TREATMENT

In the framework of the CoVER-Ab project, human monoclonal and neutralising antibodies against SARS-CoV-2 are to be extracted initially. These antibodies are then checked for their anti-viral effectiveness in cell cultures and a selection of these is then examined for effectiveness and safety in a transgenic mouse model and a rhesus monkey model.

In this study, the Preclinical Validation Unit will establish the infection model with ACE-2 transgenic mice in which the animals will be infected with different doses of SARS-CoV-2. During the subsequent effectiveness and safety testing, the antibodies are administered before and after an infection to evaluate the protection level against SARS-CoV-2.

The envisaged antibodies would then permit passive vaccination in humans - which could be used, in particular, for special risk groups until an active vaccine becomes available.

PARTNERS

- Friedrich Alexander University of Erlangen-Nürnberg (FAU) | www.nat.fau.eu
- Universitätsklinikum Erlangen (UKER) | www.uk-erlangen.de/en
- German Primate Center (DPZ), Leibniz Institute for Primate Research | www.dpz.eu/en

SUPPORT

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and Research**

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COVIDVAL – CLINICAL STUDY REGARDING THE USE OF ACE INHIBITORS AS A TREATMENT OPTION IN THE FIGHT AGAINST COVID-19

Certain drugs used to treat hypertension can also have a positive effect in COVID-19 patients. The Infectiology/Tropical Medicine, Nephrology and Rheumatology Medical Centre at Leipzig's St. George's Hospital now wants to examine this in the first controlled clinical study on this subject worldwide. For this project, the hospital will be provided with fundamental scientific support from the Fraunhofer Institute for Cell Therapy and Immunology IZI and mosaiques diagnostics and therapeutics AG, Hanover, Germany, and also from ICCAS of Leipzig University, Germany, since telemedicine support is necessary during quarantine. A study app permits the supra-regional integration of patients and simplifies processes.

Up to 20 percent of the adult German population (approximately 16 million people) are taking these drugs (of the ACE inhibitor or angiotensin receptor blocker class). In the framework of the project, the Ligand Development working group of Fraunhofer IZI is examining whether there are antibodies in patients' serums, which, in the event of a COVID-19 infection, block other important molecular structures, in addition to the known AC2 / TMPSSR binding site. Their existence could possibly explain the very different individual courses of the disease. To this end, the researchers are using a technology for examining the microstructure of the binding sites (epitopes) recognised by antibodies. It is based on peptide libraries which are presented on the surface of bacteriophages and on a special type of analysis. This permits the exact identification of the individual epitopes of the virus proteins on the amino acid, which are recognised by

the patients' antibodies. As a result, the research team is considering whether variations in the immune response might be relevant for the course of the illness. This information can help to assign patients in the study to different risk groups and then use them for diagnostics, vaccines or new drugs later on.

PARTNERS

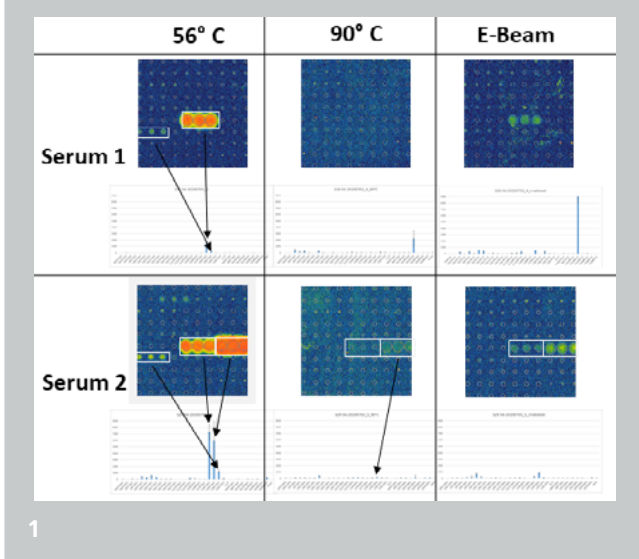
- Klinikum St. Georg, Leipzig, Germany | www.sanktgeorg.de
- mosaiques diagnostics and therapeutics AG | www.mosaiques-diagnostics.de
- ICCAS – Innovation Center Computer Assisted Surgery der Universität Leipzig | www.iccas.de/?lang=en

SUPPORT

Supported by the Saxon State Ministry of Science, Culture and Tourism (SMWK).

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COV-TOT – EXAMINATION OF THE INFLUENCE OF VIRUS INACTIVATION ON THE EPITOPE SPECTRUM IN (COVID-19) SERUMS

At present, serological diagnostics for COVID-19 are only offered based on proteins. In addition, to unexpected false positives, clinical diagnostics specifically report problems with previous infections with related Corona viruses. This is because the recognition sites of the patients' antibodies (epitopes) are only partly specific to SARS-CoV-2, while others are found in many related Corona viruses.

Therefore, in future, serological tests will also have to be developed on the basis of defined epitopes of SARS-CoV-2 or other Corona viruses which permit both simple and highly individualised diagnostics with the help of different specific and ubiquitous epitopes. The Ligand Development working group at Fraunhofer IZI has comprehensive experience in identifying epitopes directly from serums. It is already evident that SARS-CoV-2 infections lead to a strongly personalised immune response which is shaped by previous Corona infections as in the case of epitope diagnostics of food allergies (low allergen, food allergen) for various foods.

However, in all diagnostic activities, the serums obtained from infected patients are pre-treated to inactivate the virus before the serums can be used in testing. In the context of CoV-tot, it was demonstrated that different methods for virus inactivation have a very different influence on different antibodies in the sera. This can lead to very different results in serological tests in individual cases. Furthermore, the studies have shown that a slight denaturation of the sample seems to remove the blocking of individual antibodies by unknown serum components. Thus, better results can be obtained. Two methods of viral inactivation have been identified as suitable, firstly heating to 56 degrees Celsius for ten minutes for liquid

samples and secondly treatment with 70% ethanol when antibodies are immobilized on protein A.

Based on these project results, a specific diagnostic that will distinguish different corona viruses will be further developed with industrial partners. The knowledge gained in CoV-tot is also a starting point to explore differences in disease progression also in the context of clinical trials for drug treatment of COVID-19.

PARTNER

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¹ *The signal of different antibodies in the peptide array is individually and significantly reduced through pretreatment. In some cases, the antibodies can no longer be detected.*



DEFEND-COV2 – TESTING OF VACCINES AND ACTIVE AGENTS AGAINST SARS-COV-2

In the framework of the DEFEND-CoV2 project, an infrastructure for testing and evaluating vaccines and active agents against SARS-CoV-2 is to be created with the aim of giving, in particular, smaller companies, academic institutions without S3 resources and Fraunhofer Institutes the possibility to quickly test their candidates and to validate these in comparison with other technologies. At the same time, Fraunhofer's own efforts to develop vaccines and active agents are being promoted. In this process, the focus is on proprietary vaccine candidates consisting of inactivated pathogens, nucleic acids and vector vaccines. In this context, (intranasal) application through the airways is considered as an important method since a local and, therefore, potent effectiveness can be established at the virus's point of entry.

In order to be ready for the current as well as for future virus pandemics, the Immunology, Cell Therapy and GMP Process Development departments of the Fraunhofer Institute for Cell Therapy and Immunology IZI are working to build a vaccine and active agent pipeline in the DEFEND-CoV2 project. This

should also facilitate fast production for preclinical testing and the further clinical development under GMP (Good Manufacturing Practice). As a result, developers can be offered the entire value chain from preclinical testing to the production of the first clinical test specimen. This is particularly important for fast tracking as demanded by the World Health Organisation (WHO) for pandemics.

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DISCOVER 21 – HIGHLY SENSITIVE LATERAL FLOW SYSTEMS FOR THE DETECTION OF VIRAL PATHOGENS

In the disCoVer 21 project, a diagnostic test based on PCR-free detection is to be developed. This would eliminate lengthy analysis steps (transcription of RNA into DNA and subsequent PCR), which sometimes lead to long waiting times for a smear result.

Due to a shortened analysis time, infected persons can be identified, isolated and treated more quickly if necessary. At the same time, chains of infection can be better traced in order to further reduce the spread of the virus.

To simplify sample analysis and increase throughput in laboratories, disCoVer 21 targets highly sensitive lateral flow test strips on which the target substances are directly and specifically detected. From the Fraunhofer Institute for Cell Therapy and Immunology IZI the units MicroDiagnostics and Preclinical Validation are working on the project.

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DRECOR – DRUG REPURPOSING FOR CORONA

The Covid-19 pandemic is a global health emergency. Vaccines and drugs to prevent and manage infection and disease are urgently needed. Repurposing of existing drugs with known safety profiles represents a pragmatic approach to rapidly identify and develop new therapies for Covid-19. The DRECOR project team makes use of this approach.

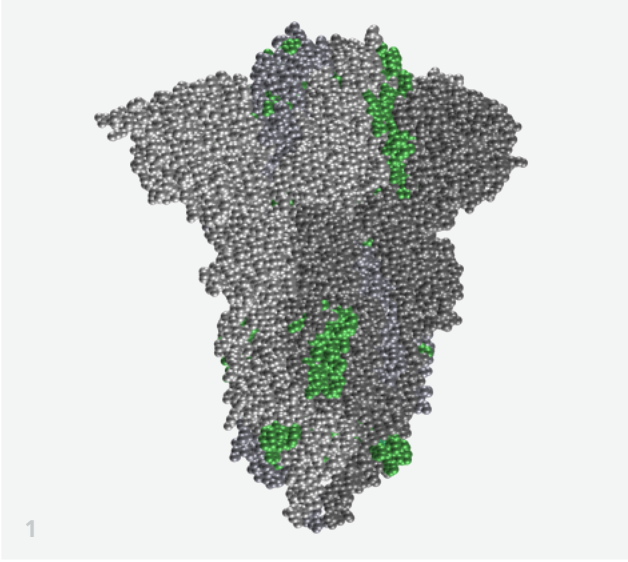
The project partners aim at generating candidate molecules formulated for inhalative administration or systemic administration targeting the airways. They will develop a device prototype for clinical development. Moreover, the DRECOR team will provide sophisticated models and test systems that can be applied to other projects and indication areas. Fraunhofer IZI will contribute its expertise in the in vivo efficacy testing of suitable drug candidates. At the end a multidisciplinary drug formulation and delivery network and process will be established within DRECOR, improving our preparedness for future pandemics.

PARTNERS

- Fraunhofer Institute for Translational Medicine and Pharmacology ITMP (Coordination) | www.itmp.fraunhofer.de/en
- Fraunhofer Institute for Toxicology and Experimental Medicine ITEM | www.item.fraunhofer.de/en
- Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB | www.igb.fraunhofer.de/en
- Fraunhofer Institute for Silicate Research ISC | www.isc.fraunhofer.de/en
- Fraunhofer Institute for Biomedical Engineering IBMT | www.ibmt.fraunhofer.de/en
- Fraunhofer-Institut für Angewandte Polymerforschung IAP | www.iap.fraunhofer.de/en
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EPICOV2020 –SARS-COV-2 SPECIFIC SEROLOGICAL DIAGNOSTICS BASED ON EPITOPES

In the serological diagnosis of COVID-19 it is a particular challenge to make a specific diagnosis against a high background of other coronavirus infections. Genome and thus proteins of the different coronaviruses are up to 50 percent identical. Efficient screening with whole envelope proteins is therefore usually always associated with the risk of a high and variable number of false positive results.

In the EpiCoV2020 project, the units Ligand Development and Cell-Functional Image Analysis of the Fraunhofer Institute for Cell Therapy and Immunology IZI and the Department of Molecular and Cellular Bioanalytics of the Fraunhofer IZI's Bioanalytics and Bioprocesses Division are working on identifying coronavirus-specific epitopes. Another project partner is the municipal hospital St. Georg in Leipzig, Germany. The project is funded by the Federal Ministry of Education and Research (BMBF).

Within EpiCoV2020, epitopes, in this case the binding sites on corona virus proteins recognized by patient antibodies, are to be identified. The epitopes, which are suitable for the specific detection of antibodies against various corona viruses, will be used in a further step to analyse sera from hundreds of patients in a clinical study (Covidval) and also from the biobank of the St. Georg hospital in Leipzig. A pre-immunization, i.e. the presence of antibodies against other corona viruses as well as the temporal development of the IgM, IgG and IgA response for individual epitopes will be investigated in this way. Not only at the end, but as soon as possible, the findings are to be transferred into a test procedure suitable for practical use, which can be produced quickly and reproducibly worldwide and thus contribute to a significantly improved serological diagnosis.

PARTNER

- Branch of Bioanalytics and Bioprocesses at the Fraunhofer Institute for Cell Therapy and Immunology IZI | www.izi-bb.fraunhofer.de/en
- Klinikum St. Georg, Leipzig, Germany | www.sanktgeorg.de

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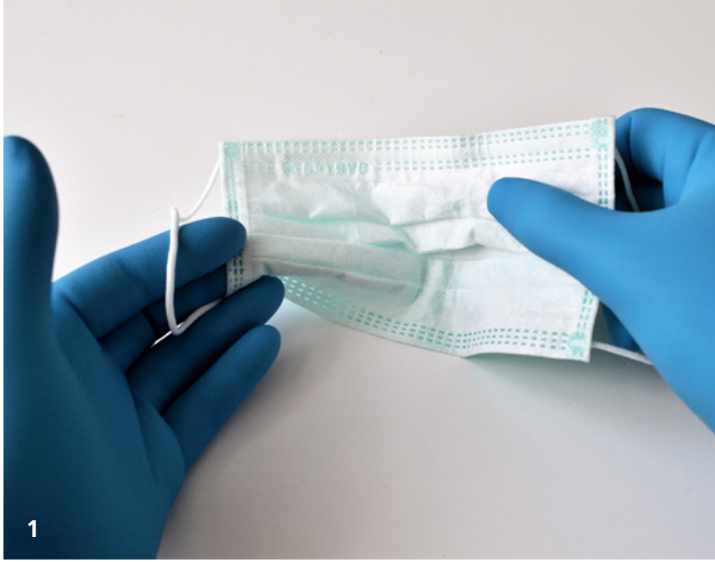


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1 *The S-protein found on SARS-CoV-2 consists of three identical subunits. Some of the most important epitopes recognized by patient antibodies are marked green.*



SENSE-COV2 – ANALYSIS OF THE INNATE IMMUNE RECOGNITION OF SARS-COV-2 USING RECOMBINANT VIRUSES

Containment of the corona pandemic is hampered by a significant proportion of infected persons showing very few or no symptoms. The fact that SARS-CoV-2 is able to multiply without signs of inflammation suggests that innate immune control against SARS-CoV-2 may be deregulated and less effective.

Within the framework of the SENSE-CoV2 project funded by the German Federal Ministry of Education and Research (BMBF), the research team aims to characterize mechanisms that enable SARS-CoV-2 to escape detection by the human innate immune system.

The identification of viral proteins that prevent early immune control and their characterization in infection experiments will provide important foundations and new target structures for a possible development of antiviral drugs aiming at improved control of the virus by the innate immune system.

PARTNER

Friedrich Alexander University of Erlangen-Nürnberg (FAU) | www.nat.fau.eu

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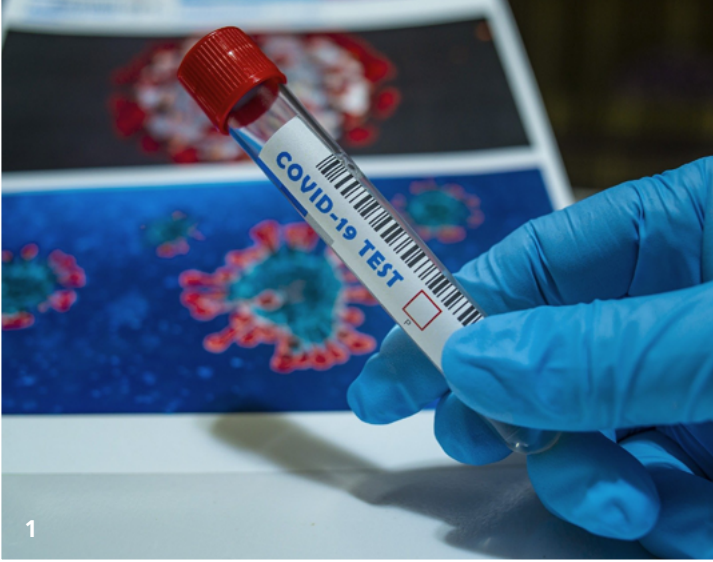
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1

SAXOCOV – SAXON COVID-19 RESEARCH CONSORTIUM OF NON-UNIVERSITY, UNIVERSITY AND CLINICAL PARTNERS

The consortium conducts a Saxony-wide field study on the spread of SARS-CoV-2. It is supported by two further, non-Saxon research institutes. The aim is to create a scientific instrument to follow the development of the SARS-CoV-2 epidemic in the German Free State of Saxony on multiple levels. The field study will on the one hand serve to monitor the effectiveness of governmental measures to contain the pandemic and on the other hand support the detection and limitation of outbreak scenarios. The sound knowledge base thus created will enable predictions to be made about future developments and help to assess the effectiveness of containment measures.

The samples and data collected in the field study will also be used in an accompanying research study to answer further research questions. In particular, the question is pressing as to which causes are responsible for the very different mild or aggressive course of the disease and whether there are parameters with which these different courses can be predicted.

More information: www.saxocov.de (in German only)

PARTNERS

- Faculty of Medicine, Leipzig University, Leipzig, Germany | www.uniklinikum-leipzig.de
- Helmholtz Centre for Environmental Research – UFZ, Leipzig, Germany | www.ufz.de
- Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany | www.mpi-cbg.de/en

- Faculty of Medicine, TU Dresden, Dresden, Germany | www.tu-dresden.de/med/mf
- Städtisches Krankenhaus Sankt Georg, Leipzig, Germany | www.sanktgeorg.de
- Hannah Arendt Institute for Totalitarianism Studies, Dresden, Germany | www.hait.tu-dresden.de
- Wrocław University of Science and Technology, Wrocław, Poland | www.pwr.edu.pl/en
- University of Münster, Institute of Epidemiology and Social Medicine, Münster, Germany | www.medicin.uni-muenster.de/en/epi/welcome-to-the-institute-ofepidemiology-and-social-medicine

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The measure is co-financed with tax funds on the basis of the budget approved by the Saxon State Parliament.

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VIRENWOLF – VIRUCIDAL TUNGSTEN CARBIDE-BASED COMPONENT SURFACES FOR INTENSIVE MEDICAL AND NURSING CARE FACILITIES

Respiratory infectious diseases are seen as one of the greatest risks for the current and future pandemics. Droplet and aerosol-based transmission routes of respiratory viruses such as SARS-CoV-2 usually occur directly via the mucous membranes of the nose and mouth. The indirect route is via surfaces on which infected persons sneeze and leave behind fluid particles with a high bacterial count that can infect other people. Especially in clinical environments or in nursing, it is of particular importance to interrupt infection paths via surfaces contaminated with aerosols. Particularly affected are storage surfaces and castors of tables for instruments, care dressing material etc.

In order to prevent these infection paths, the Fraunhofer Institute for Ceramic Technologies and Systems IKTS and the Fraunhofer Institute for Cell Therapy and Immunology IZI are collaborating in the VirenWolf project. The Fraunhofer IKTS is initially developing a process for producing inexpensive, large-area and abrasion-resistant virucidal and antibacterial surfaces by means of thermal spraying. The virucidal effect of tungsten carbide has already been demonstrated in preliminary tests at the Fraunhofer IKTS. However, this has not yet been implemented in materials or coatings, as conventional coatings contain cobalt, which is classified as carcinogenic. The project team therefore focuses on developing tungsten carbide coatings with copper-containing solution-resistant binders. Their virucidal effectiveness will then be tested at Fraunhofer IZI. The scientists will examine the most effective materials for potential cytotoxic effects with regard to the compatibility of people handling them.

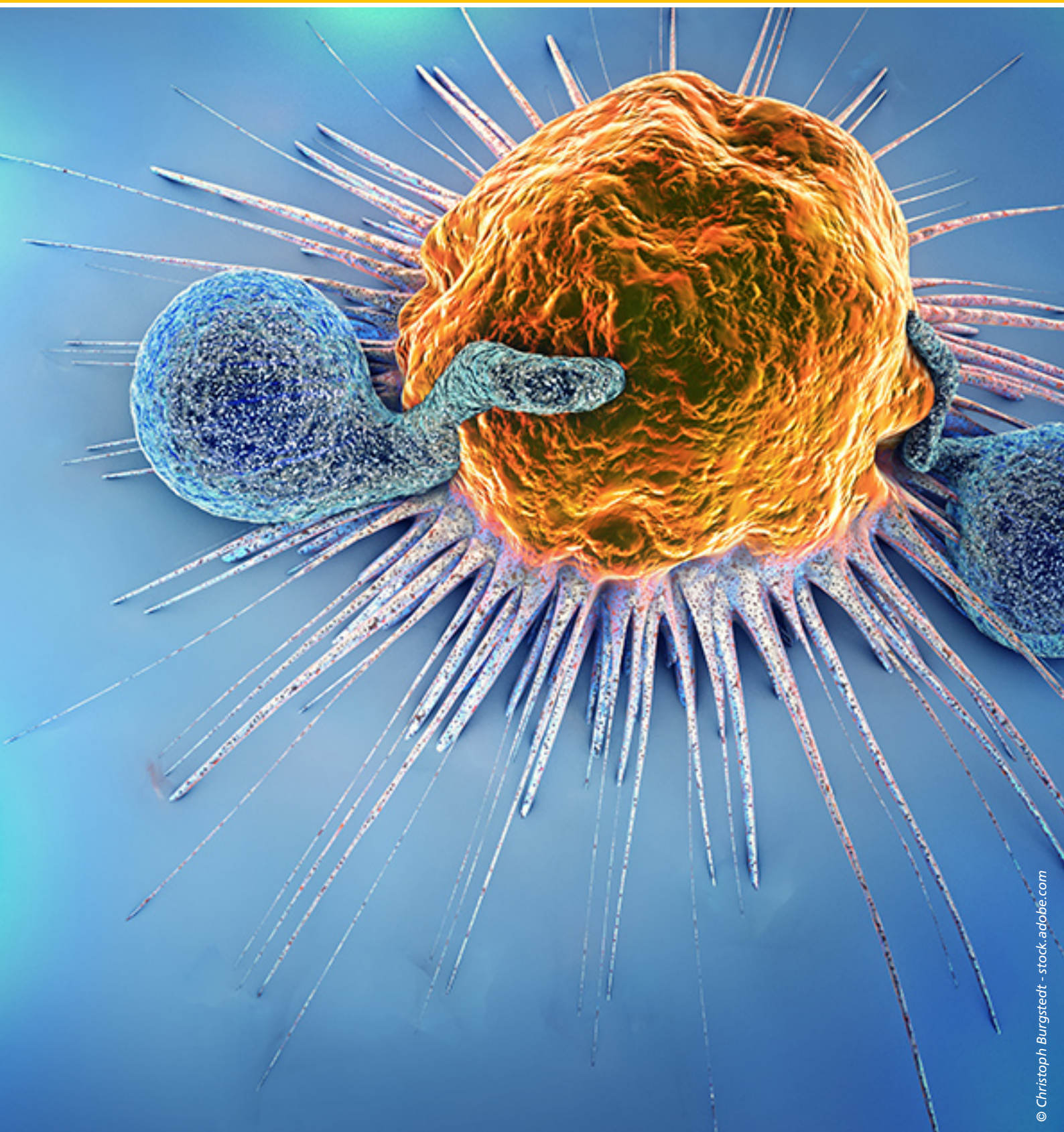
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IMMUNO- ONCOLOGY





1



2

MANUFACTURE OF KYMRIAH®

The 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 collected 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 through 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 of these indications based on the recommendation given by the European Medicines Agency (EMA).

Fraunhofer IZI has long been an important manufacturing and development site for this innovative CAR-T cell therapy for clinical trials throughout Europe. Currently, prescription-only, approved T-cell therapies will also be manufactured on an interim basis in the Main Department of GMP Cell and

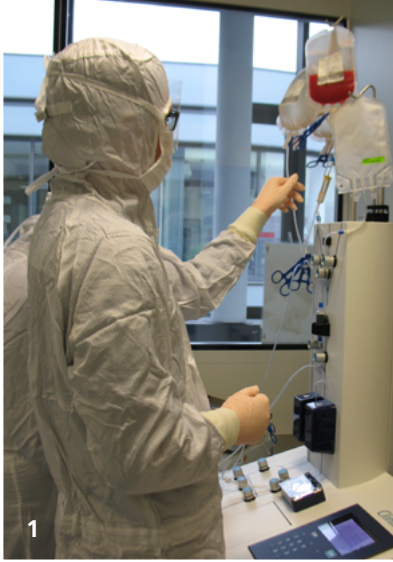
Gene Therapy at Fraunhofer IZI, alongside investigational medicinal products. Following a one-year technology transfer period from Novartis' Morris Plains site in New Jersey, USA, and after obtaining manufacturing authorization in accordance with Section 13 of the German Drug Act (AMG), the first clinical batch was manufactured at Fraunhofer IZI in Leipzig in August 2016. Since then, the Main Department of GMP Cell and Gene Therapy has continuously produced CAR-T cell therapies for Novartis.

Until the end of 2020, several 100 batches 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 automated manufacturing equipment, 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.

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



POC INITIATIVE ROR1 CAR-T

In 2017, CAR-T cell therapy was the first ever gene therapy to be approved by the US Food and Drug Administration (FDA). The treatment has since attained impressive outcomes in clinical trials involving cancer patients. This revolutionary form of therapy also lies at the heart of the “ROR1 CAR-T” research project. The chimeric antigen receptor (CAR) developed at the University Hospital of Würzburg recognizes the ROR1 molecule, which is expressed in cancer cells in leukemia, for example, as well as in breast and lung cancer. In order to manufacture the cell product, immune cells are taken from the patient’s body by means of leukapheresis. T helper cells and cytotoxic T cells are then selected by magnetic cell separation. The genetic material for the CAR is introduced into the genome of the T cells via a non-viral gene transfer using the “Sleeping Beauty” transposon system (jumping gene). This reprograms the T cells in such a way that they perceive ROR1-positive cancer cells as “foreign” and eliminate them by releasing cytotoxic messengers. The reprogrammed cells are in vitro expanded and administered to the patient intravenously. The project is being funded as a pilot project under the proof-of-concept initiative initiated by the Fraunhofer-Gesellschaft, the Helmholtz Association and Deutsche Hochschulmedizin in order to promote the translation of innovative research projects. The funding will support the conduct of preclinical trials into the safety and efficacy of the ROR1 CAR-T cells and drive clinical translation into a phase I/II study (first in man). Test batches were produced in the project to begin with; these batches were

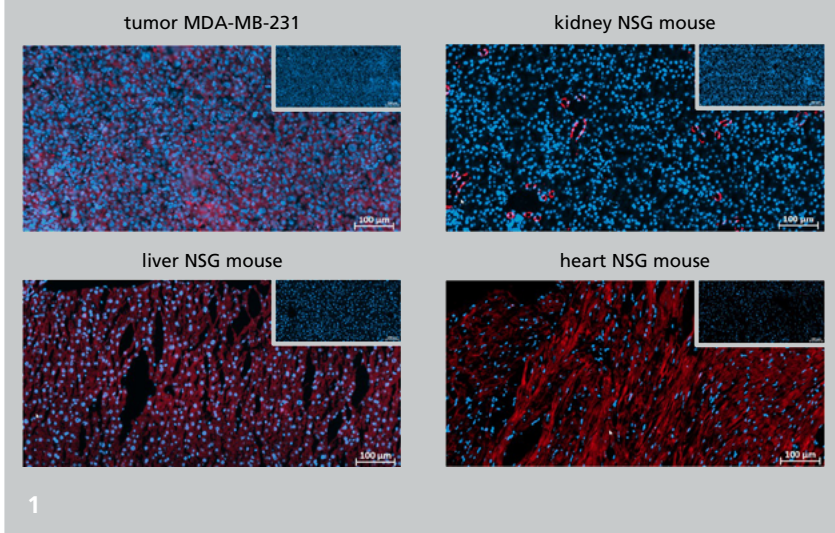
used to optimize the process with regard to the stringent production requirements under GMP conditions and to qualify the required equipment. After successfully establishing the process and determining the necessary specifications, several validation batches were produced in the clean room and analytical testing commenced. A final validation run is planned for the first quarter of 2021. The samples generated in these validation batches will also be used to validate the analytical methods that go into the safety parameters (mycoplasmas, sterility, bacterial endotoxins, transposon copy number). An application will be made to the competent authority, Landesdirektion Sachsen to include the investigational medicinal product under the existing manufacturing authorization pursuant to Section 13 of the German Medicinal Products Act (AMG) once the validations are complete.

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1 Loading the tubing set for selection onto the *CliniMACS Plus*.

2 Preparing for transfection with the *MaxCyte GTX*.



POC INITIATIVE ROR1 CAR-T: A PRECLINICAL GLP STUDY TO VERIFY THE SAFETY OF A CAR-T CELL THERAPY THAT TARGETS TYROSINE KINASE-LIKE ORPHAN RECEPTOR 1 (ROR1)

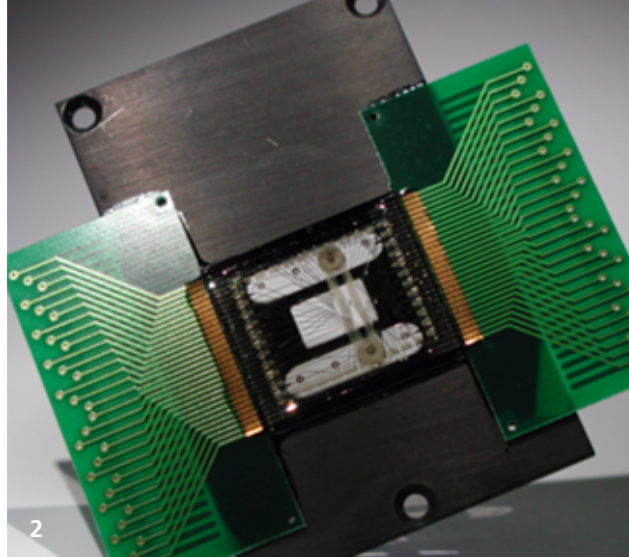
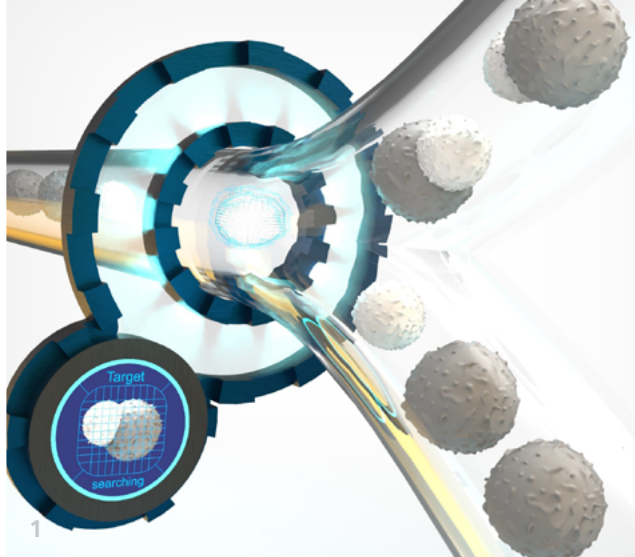
Current oncology research is looking at mobilizing the immune system to fight tumors in the long term. Promising immuno-oncology drugs are ready to be used in various tumor indications. In addition to activating the immune system through antibodies, the approach of adaptive T-cell therapy in particular presents another encouraging strategy. The first T-cell therapy to express a chimeric antigen receptor (CAR) was authorized in the USA in 2017. Since then, a number of impressive clinical successes have been achieved in the field of hematological cancer. A project funded as part of the proof-of-concept (PoC) initiative instituted by the Fraunhofer-Gesellschaft, the Helmholtz Association and Deutsche Hochschulmedizin concentrates on developing an additional tumor target for treating hematological and also solid tumor indications. CAR-T cells designed to target surface molecule ROR-1 are to be used to address hematological tumors such as mantle cell lymphoma besides solid tumors such as breast and lung cancer. ROR-1 is a tyrosine-protein kinase transmembrane receptor which is strongly expressed during embryonic development, but rarely on healthy adult cells. An extremely high level of ROR-1 expression was able to be detected on mantle cell lymphoma tumor cells as well as in the case of breast cancer and lung cancer. In the research project funded through the PoC

initiative, a non-viral gene transfer ensues through the “Sleeping Beauty” transposon system (SB100X) developed at the Max Delbrück Center for Molecular Medicine (project partner). Moreover, besides establishing manufacturing and quality assurance processes (Main Department of GMP Cell and Gene Therapy), preclinical GLP studies are also being conducted at Fraunhofer IZI to verify the safety and efficacy of the ROR-1 CAR-T cell therapy (Department of Preclinical Development and Validation) in order to ensure that the prerequisites for starting the clinical trial are fulfilled.

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1 *Formalin-fixed paraffin-embedded tissue sections from a tumor induced by the TNBC cell line MDA-MB-231 or from selected normal tissues (kidney, liver, heart) of an NSG mouse. ROR-1 (red) was tagged by indirect immune fluorescence, while the nuclei were counterstained by the DNA fluorescent dye 4',6-Diamidin-2-phenylindol (DAPI; blue).*



HIGH-THROUGHPUT IMAGE-BASED CELL SORTING

The characterization and separation of heterogeneous cell samples is a cornerstone of modern biomedicine and is becoming increasingly important as a key technology for cell-based therapies. To provide cells in high purity, different cell types of a heterogeneous sample have to be identified and separated from the remaining cells. Nowadays, this is mainly done by fluorescence- and magnetic-activated cell sorting (FACS, MACS), where the different cells are identified by the presence or absence of specific marker molecules. However, this approach falls short for many sorting applications in medicine and biotechnology as the functionality of many cell types is not primarily mediated by the presence or absence. A number of cell types are mediated by the local distribution of these molecules within the cell, as well as other, spatially resolved features: Thus, activation and differentiation processes in stem and immune cells are accompanied by co-localization and the redistribution of certain immune checkpoints and transcription factors, respectively. Effector cells directed against cancer can be identified by their binding to tumor cells, and efficient producer cells of biofuels can be detected by the number and size of intracellular lipid vesicles. Such parameters cannot be measured by FACS or MACS, but only by imaging analysis, and can be used for cell sorting.

The aim of this cooperation project between Fraunhofer IZI-BB, IOF, IIS and the Charité Berlin is to establish a flow-through method for image-based sorting of cells in high throughput, which is based on the worldwide unique microfluidic systems of the IZI-BB. In this process, cells flow

through parallel micro-channels while their (fluorescence) microscopic image information is acquired (IOF) and classified almost instantly using intelligent and adaptable image analysis software (IIS). The sorting decision is transferred to the target cells immediately by means of electro-kinetic forces, deflecting them from their path and depositing them in provided microwells.

The biomedical validation of the method is performed in close collaboration with the Berlin Institute of Health (BIH) of the Charité Berlin around Prof. Volk and Dr. Schmück-Henneresse. We will use the system to isolate rare immune cell stages, which are important for anticancer immunotherapy, to perform single cell genome analysis. A better understanding of the immune response behavior of these cells will enable the optimization of corresponding cell products in adoptive immunotherapy.

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- 1 *Graphical representation of the sorting process.*
- 2 *Microfluidic system for high-precision cell handling.*

INFECTION RESEARCH





WORKING WITH HIGHLY PATHOGENIC VIRUSES

Fraunhofer IZI has operated a biological safety level 3 laboratory since 2016, where work can be carried out using highly pathogenic disease agents. This S3 laboratory is hermetically sealed from the outside world and also has a negative air pressure system permanently in place, ensuring no air can escape in the event of an accident. This infrastructure allows Fraunhofer IZI to handle special projects in the field of infectiology. A focal area here is recently emerging viruses, especially those transmitted by insects.

Since mid-2020, for example, work has been carried out on the EU-funded project FLAVICURE, which aims to identify active agents that can be used to fight West Nile virus. In cooperation with industry partners Protinhi Therapeutics (Holland) and Chimera Biotec (Germany), a high number of substances will be tested for efficacy against the pathogen. West Nile virus is transmitted by mosquitoes and is now also endemic in Germany. Other projects look at ways of detecting and combating dengue and Chikungunya viruses. Since March 2020, a huge amount of work has also involved the novel coronavirus SARS-CoV-2. As an airborne pathogen, this virus places even greater demands on safety in the laboratory. Members of staff wear protective ventilator hoods featuring portable, motorized filter systems. The institute is involved in a number of coronavirus-related projects. The project partners here are mainly pharmaceutical companies,

while the projects themselves center around the efficacy testing of vaccines and drugs. Testing the antiviral efficacy of certain materials, e.g. those used in means of transport or hospital facilities, also forms an important field of work. Moreover, research is being conducted into the immune response of Covid-19 patients in cooperation with Leipzig-based Klinikum Sankt Georg community hospital (see SaxoCov project on page 72).

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BREATHALERT – DETECTION OF ANTIBIOTIC-RESISTANT BACTERIA USING ION MOBILITY SPECTROMETRY

In a report, the World Health Organization emphatically describes why the fight against antibiotic resistance is one of the major tasks faced by the global community. By the year 2050, the organization expects 10 million deaths annually that will be attributable to infectious agents [1]. Innovations are necessary not only for therapeutic treatment, but also for the diagnostic detection of pathogens that cause disease to counteract the challenge in the healthcare sector.

The BreathAlert project launched at the end of 2020 aims at improving this situation with a new method for the rapid and non-invasive detection of infectious agents and antibiotic resistance, which analytically analyzes patients' breath. The project focuses on the further development of ion mobility spectrometry, which is to be used to characterize volatile organic components (VOCs) of microorganisms.

At the Fraunhofer IZI, selected microorganisms are being examined to determine whether they can be differentiated via the VOCs released and whether they can be assigned to the respective types of bacteria. For this purpose, the pathogens are first cultivated and then the headspace, the gas phase above the culture medium, is fed into the device. The VOCs are ionized, separated in an electric field and then detected at different times. Software analyzes the complex data. The aim is to identify specific signals with which bacteria can be reliably differentiated from one another, even under different conditions. The focus is on antibiotic-resistant pathogens, such as enterobacteria, which are increasingly showing resistance to carbapenem and cephalosporin [1].

The characterization of clinical isolates, air samples from infected patients and measurements of the influence of e.g. eating habits on the air we breathe round off the project.

The company Graupner medical solutions GmbH, which develops the medical device technology, works together with the Fraunhofer IZI as a consortium partner. The development work is supported by specialist clinics that provide access to samples and also carry out a final validation. The project results are used economically by the Graupner company.

1] World Health Organization Report 2017: Prioritization of Pathogens to guide discovery, research and development of new antibiotics for drug-resistant bacterial infections, including tuberculosis. WHO/EMP/IAU/2017.12

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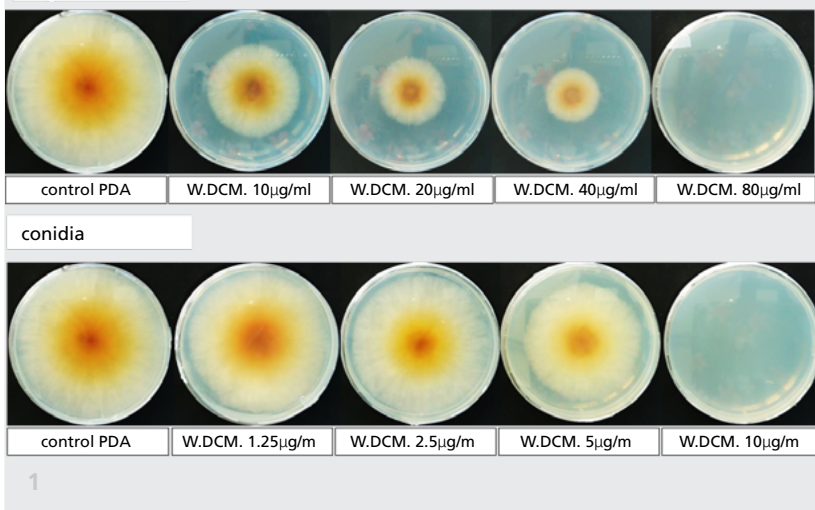


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1 VOCs in human breath (from article:
A. Dan Wilson. Atlas of Science. 2016 Feb 29).



DEVELOPING BOTANICALS-BASED PESTICIDES TO FIGHT PHYTOPATHOGENIC FUNGI IN AGRICULTURE

Most agricultural crops are attacked by a variety of pathogens, usually viruses or fungi. As their cultivation and selection is based solely on high returns, many crops have lost the ability to protect themselves effectively against pathogens. Until now, conventional fungicides have been successful in tackling harmful fungi. However, restrictive limits on the amounts of fungicide that can be used together with the fact that commercial fungicides tend to contain just one active ingredient have led to many harmful fungi developing resistances in recent years, resulting in severe crop losses.

Active ingredients garnered from tropical plant extracts may offer a way out here. Tropical plants, especially trees, have formed a large number of active ingredients through a process of co-evolutionary adaptation that offer effective protection from fungal infections and pests. A huge advantage of plant extracts lies primarily in the fact that they normally contain several active ingredients which often work together. As the active ingredients of one extract simultaneously have an inhibitory effect on different enzymes / enzyme complexes or components of the fungal cell membrane and/or cell wall, it becomes much more difficult for harmful fungi to develop resistance than in the case of a monosubstance-based, conventional fungicide.

The aim of this research project was to test the fungicidal effect of the plant extracts compared with conventional active agents in a realistic study.

As part of a joint project with Makerere University (Kampala, Uganda) and the IRGIB (Cotonou, Benin), a total of 33 extracts was produced from the leaves, fruits and barks of

different plants and tested both in vitro on different species of harmful fungi (e.g. *Botrytis cinerea*, *Fusarium graminearum*, *Colletotrichum graminicola*) and ad planta (e.g. on corn, apples and grapevines).

The results confirmed that the plant extracts were not only as effective as commercial agents – in some cases they were even superior. The extracts were shown to offer huge advantages above all in fighting resistant and multiresistant harmful fungi. Moreover, the tested botanicals demonstrate good rain resistance and high UV stability.

Based on these results, utilization strategies are being developed with the African partners to drive forward the commercialization of several concepts in the form of sustainably produced and ecologically compatible pesticides.

SUPPORT

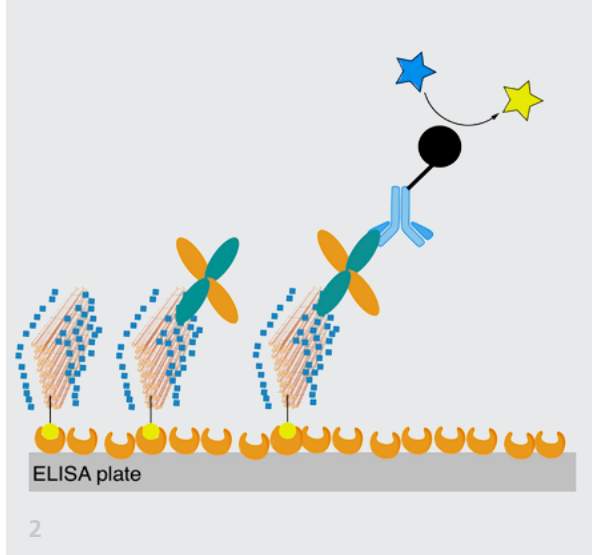
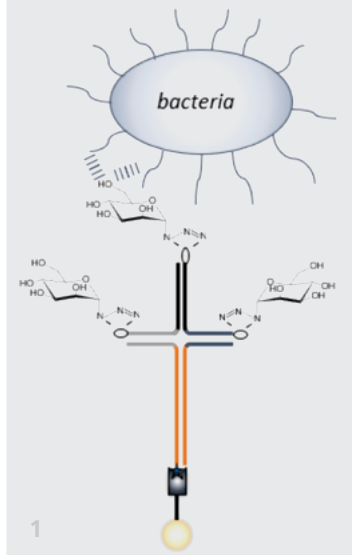


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Agriculture and Food

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1 *Illustration of how a plant extract can help tackle the conidial and mycelial growth of harmful fungi.*



GLYCO3DISPLAY: DNA-TEMPLATED ASSEMBLY OF GLYCANS FOR DEVELOPING NOVEL PATHOGEN ANTI-ADHESIVES

Polysaccharides, also known as glycans, are long and complex sugar molecules made up of a chain of monosaccharides such as mannose, glucose or fructose. Numerous glycans are found on the surface of human cells, and are used by disease-causing bacteria or viruses as molecules for recognizing, binding, and eventually infecting the host cells. Therefore, sugar molecules such as mannose, heparin or sialic acid, which are found on the membrane of human cells, are particularly interesting from a medical research perspective. Nanometer-scale geometry also plays an important role here; viruses and bacteria exploit the principles of multivalence, where two or three sugar-binding receptors act cooperatively to more efficiently bind to and infect their targets.

In Glyco3Display, novel carbohydrate-based compounds are created by integrating different glycan molecules with DNA-based structural scaffolds. The approach allows precise arrangements of defined glycan chains with single-nanometer spatial resolution to be established. This brings together two key technologies from the partners Fraunhofer IZI and the Max Planck Institute for Colloids and Interfaces: DNA Nanotechnology and Automated Glycan Synthesis.

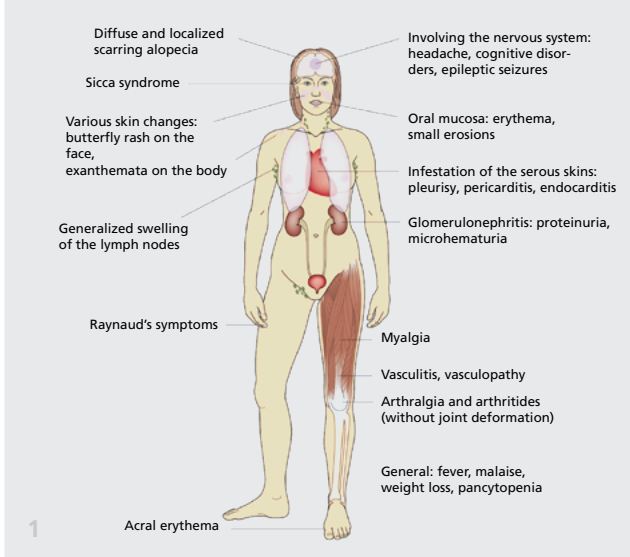
One part of this project focuses on creating high-throughput assays for investigating the binding of specific glycan formulations and arrangements to target pathogens or glycan-binding proteins. For this, glycosylated DNA nanostructures have been integrated into two standard, analytical platforms that are widely accessible to researchers around the world.

First, by integrating the DNA-glycan compounds onto microbeads, any standard automated flow cytometry system can be used to quantify the impact that the exact glycan composition and how they are geometrically arranged on DNA scaffolds has on their ability to bind the surface of the pathogen. Alternatively, we different types of DNA-glycan nanostructures with the hardware used for carrying out classical ELISA assays. Thus, synthetic replacements for antibodies used to capture and detect in immune-diagnostics were created. Unlike standard ELISAs or other similar assays, this method allows rapidly screening through many candidate ligands, and additionally controlling the geometric arrangement in which they are presented to targets proteins.

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- 1 Sugar molecules are conjugated to small, branched DNA structures formed from 4 individual DNA strands. When bound to magnetic beads, these can be used for the high-throughput screening of how compounds bind to bacteria like *E. coli*.
- 2 Close to 100 sugar molecules are conjugated to large "DNA origami" nanostructures, formed from several hundred DNA oligonucleotides. When integrated into ELISA plates, these can replace standard antibodies used to capture or recognize targets in immuno-diagnostics.



STUDIES ON THE INFECTIVITY OF DIFFERENT PATHOGENS (INFLUENZA A VIRUS, RESPIRATORY SYNCYTIAL VIRUS) USING LOW DOSE INTERLEUKIN-2 IMMUNOTHERAPY AGAINST LUPUS ERYTHEMATOSUS

Systemic lupus erythematosus (SLE) is an autoimmune disease. In SLE patients, chronic inflammatory processes occur throughout the whole body. Worldwide, approximately 5–8 % of the population is currently affected by various autoimmune diseases. They form the third most common group of diseases after cardiovascular diseases and tumors. A central role is played by a disorder in the immune system leading to a loss of tolerance to the body's own tissue structures. The immune system, can no longer distinguish between "foreign" and "self" (auto). As a result, the immune system attacks healthy, endogenous tissue. Since a cure of the disease is not possible, corresponding therapies aim at lowering the autoimmune reaction. However, such immuno-suppressants such as cortisone are not really suitable for long-term therapy because of their toxicity. Similarly, lowering the immune response increases susceptibility to various pathogenic agents and infections.

One aspect in SLE patients is the decreased IL-2 production. This leads to a variety of immuno-deficiencies such as reduced T cell production and functionality. It is known that regulatory T cells (Treg) play a central role in maintaining immunological tolerance. A deficiency of Treg cells increases the susceptibility to autoimmune diseases (e.g. SLE or multiple sclerosis). However, if Treg cells predominate, there may be an increased susceptibility to infection due to their ability to suppress T- and B-cell responses. Since IL-2 therapy to regulate the number of Treg cells is a promising therapeutic modality for treating SLE patients, the safety of this therapy must be tested with regard to increased

susceptibility to infection using an in vivo model as part of the imSAVAR project. Therefore, an SLE model (i) will be established and the therapeutic effect of different IL-2 doses will be investigated (ii). Finally, the susceptibility to influenza A or RS viruses and occurring side effects in their type, frequency and incubation period will be documented in this SLE mouse model, and the viral load in the animals will be determined (iii). This will allow conclusions about the possible increased vulnerability to infections under IL-2 treatment compared to the control groups. The long-term goal is to create a prediction platform for different pathogens in patients with IL-2 therapy.

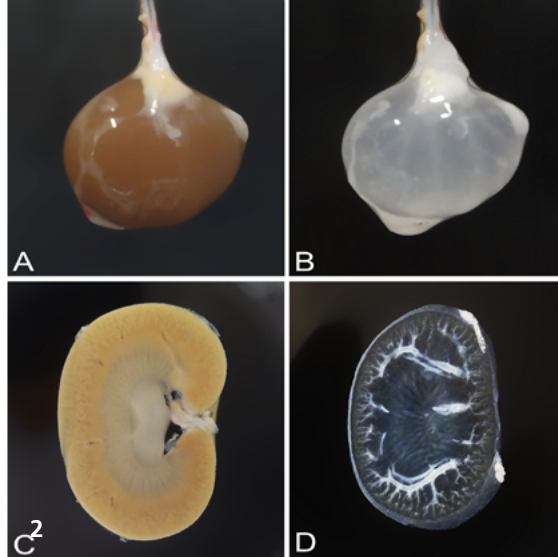
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¹ *In addition to the skin, other organs such as the heart, lungs and kidneys are also often seriously damaged in SLE patients. (Moll, Duale Reihe Dermatologie, Thieme, 2016).*

FURTHER SELECTED PROJECTS





3D RENAL TISSUE MODELS

Around ten percent of the world's population is affected by chronic kidney disease. Current treatment options comprise dialysis and kidney transplantation, however neither of these are satisfactory from a medical or patient perspective for many reasons. The prospect of a third option in the future in the form of synthetic (bioartificial) kidneys would therefore be hugely appealing to medics and patients alike. Several impressive advancements have already been made based on research approaches in the field of tissue engineering, however the path to functioning kidneys remains long.

This project focuses on establishing tissue model systems that can then be used to more specifically address a range of issues relating to the efficient decellularization and subsequent recellularization of kidney tissue taken from rats. After removing the animal cells, an extracellular matrix (ECM) remains in the form of a delicate, anatomically intact scaffold that can then be populated with human cells. The processes involved in both removing the original cells and repopulating the scaffold with human cells are, however, complicated and require a great deal of fine-tuning. The main decellularization technique used to date is organ perfusion based on chemical reagents, yet this can significantly impair the quality and integrity of the remaining scaffold. This project will be the first to look at the application of hydrostatic high-pressure treatment (HHD) on the decellularization process. HHD can lead to a rapid and effective devitalization of cells, making subsequent perfusion shorter and therefore less damaging for the ECM. This would be hugely beneficial for recellularization. Besides intact kidneys, precision cut kidney sections are also being examined here as they are extremely well suited as 3D tissue model systems.

These types of tissue model are ultimately to be used to address a number of questions, from the precise examination of the cellular and molecular processes involved in recellularization, over to functional analyses of nephrons, right through to pharmacological matters. The project is being funded as part of the Excellence Initiative of the Federal State of Mecklenburg-Vorpommern (HOGEMA consortium). Fraunhofer IZI's Rostock-based work group Extracorporeal Therapy Systems is involved in a research alliance looking at tissue replacement materials together with the University of Rostock, University of Greifswald and Wismar University of Applied Sciences.

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- 1 *Preparing the kidneys.*
- 2 *Intact kidneys and kidney sections before and after treatment.*



ANTIBODIES FOR THE TREATMENT OF NEURODEGENERATIVE DISEASES

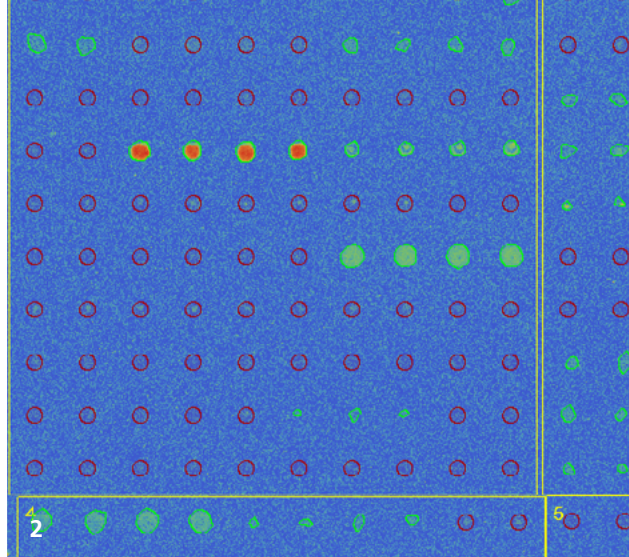
Neurodegenerative diseases are characterized by the progressive loss of brain substance. The degeneration of nerve cells coincides with the development of dementia, i.e. a qualitative and quantitative decline of brain cognitive performance. Due to the rise of life expectancy, dementia, especially Alzheimer's 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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AUTOMATED ANALYSIS OF PEPTIDE-MICRO-ARRAYS

Micro-arrays as molecular biological screening systems contain thousands of tightly packed tests (spots) on an object slide. Fluorescence microscopy images of these slides can be automatically analyzed with commercially available software solutions. However, this requires a great number of spots that should have a high signal intensity whereas no interfering artifacts are present in the image. If these conditions are not met, the hitherto existing software does not automatically detect the spots, which increases the need for time-consuming manual analysis.

During the development phase of a particularly sensitive micro-array-screening-system, the prototypes may exhibit only a small count of high intensity spots, on top of that with a low signal to noise ratio (SNR). To enable high throughput testing for these images, the Image Analysis of Cell Function Unit and the Ligand Development Unit develop robust algorithms for the detection and segmentation of spots. Using a prototypical software implementation, and by introducing the new option of exporting some statistical parameters, the processing time per sample could be remarkably reduced compared to manual analysis.

Going beyond the current project EpiCoV2020, the algorithms could be tested successfully for images of peptide micro arrays obtained from allergy research. The main goal is now to evaluate more cases of application and to implement the algorithms in a distributable software.

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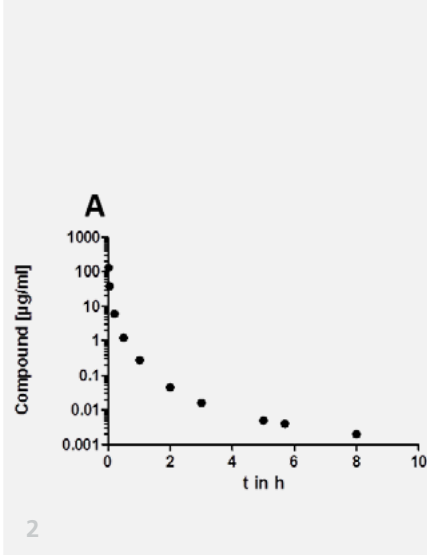
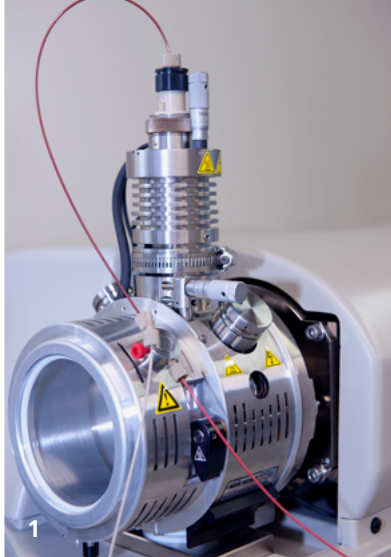


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- 1 Section of a peptide-micro-array after adjusting the intensity and annotation of the robust detection of single spots.
- 2 Same section with the annotation of the segmentation result.



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.

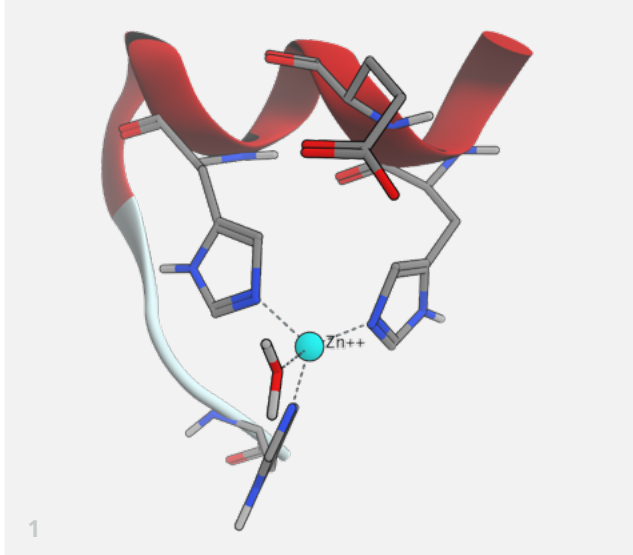
The Department of Drug Design and Target Validation at Fraunhofer IZI develops new molecular therapies for neurodegenerative and inflammatory disorders. The department's strategy includes identifying novel drug target and testing novel therapies. For characterizing new small molecule classes, a catheter-based 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|2 Mass spectrometry analysis to determine the concentration of the active ingredient in the organism (A).



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.*



MAPPING OF SERA FOR EPITOPES OF ALLERGY-RELATED ANTIBODIES

LowAllergen started in 2013, the first project in the group focused on identifying epitopes of allergenic soy proteins. Today, after completing the follow-up project FoodAllergen, a full spectrum of validated epitopes covering several food allergens has been established. By the end of 2019, a new ERAnet project (POC4Allergy) began with the development of alternative Point of Care (POC) tests in collaboration with the Charité in Berlin and partners in France and Romania.

Immunodiagnosics for diseases are currently based mostly 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 are difficult to distinguish, as commonly observed for influenza viruses. Protocols have been established to exactly identify the antigen's sites where patient antibodies bind (epitopes), which can also be investigated directly using patient sera. This allows the reliable identification of the pathogen, the causative antigen of allergies, or other indications such (auto)immune or infectious diseases (COVID-19) as well as novel approaches for therapy and research.

The group's research has focused on food allergies over many years. A steady increase of patients could be observed in recent years. Cross reactivities between food allergens reduce the reliability of common allergy tests. Epitope-based diagnostics are probably the only alternative to costly clinical

examinations. Oral food provocation still remains as the gold-standard for the diagnosis of food allergy, which has to be carried out under medical supervision in a clinic. An efficient diagnosis, appropriate treatment and dietary adjustments are therefore not available for many patients.

FoodAllergen was a particularly large project and was followed with great interest by local and international allergologists. In cooperation with several other Fraunhofer Institutes and hospitals, the FoodAllergen project aimed at dealing with food allergies using a holistic approach. This comprised the identification of allergens in foods and new processes of producing food ingredients with reduced allergenic potential. Epitopes for 14 plant allergens have been identified and many of them have already been validated with more than 200 sera from the Fraunhofer IZI Allergy Biobank. From these epitopes, the European project POC4Allergy focuses on hazelnut- and peanut-epitopes able to discriminate between sensitization and a severe, life-threatening allergy.

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miRNA ANALYSIS OF PATIENTS WITH CHRONIC PAIN

Chronic pain is a serious health issue affecting around a fifth of the European population. The efficiency of treatment is limited by a lack of options. Chronic pain is accompanied by abnormal neuronal activity in the central nervous system and results in hypersensitivity of the nociceptive system. The first link in a complex “chronification chain” is peripheral sensitization following mechanical or inflammatory damage to the peripheral nerve structures. This involves the release of several inflammatory mediators. Most of the soluble factors here are pro-inflammatory cytokines. Recent studies are analyzing biomarkers such as cytokines or microRNAs in search of reliable markers for the chronification of pain. Previous investigations in the field of chronic pain focused on analyzing sensory nerves in affected tissue. Addressing miRNAs in serum as potential markers adds a whole new dimension to this complex picture. The work undertaken at Fraunhofer IZI-BB aims to characterize miRNA in serum samples taken from polyneuropathy and/or radiculopathy patients. By measuring specific electrophysiological profiles in order to detect functional disorders of the sensory system at an early stage, patients can be specifically classified and assigned to corresponding groups. This classification, or stratification, based on objectified parameters allows investigations to be carried out on a well described patient cohort and therefore offers a considerable advantage over previous studies. This opens up the possibility of identifying individual analytes or groups of analytes such as miRNA or cytokines; a possibility which had never been an option in the past due to a lack of objectified parameters on which to base stratification. Following the bioinformatic evaluation of all the

data in the consortium, specific markers can be identified and transferred to a potential platform for point-of-care analysis. As part of the bioinformatic evaluation, the measured parameters are examined individually and in combination with respect to their predictive value, specificity and selectivity.

The project forms part of the NoChro consortium funded by the Federal Ministry of Education and Research.

SUPPORT

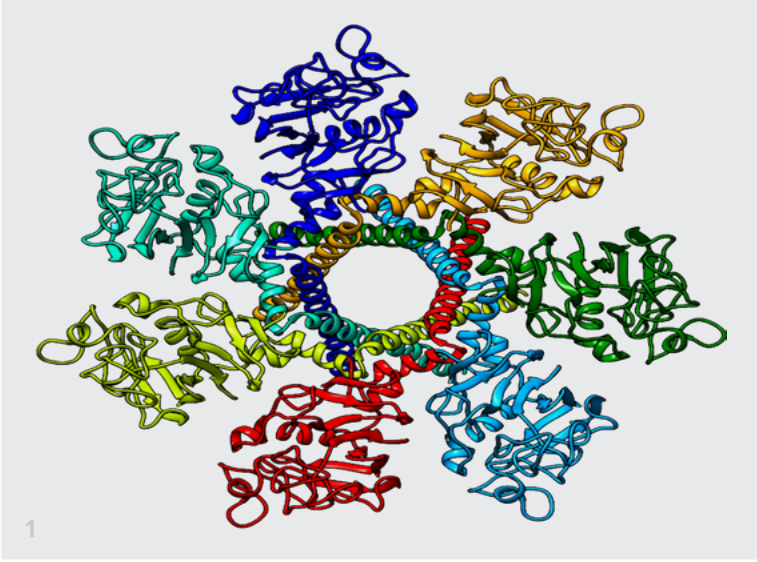
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PROCESS DEVELOPMENT, MANUFACTURING AND QUALITY CONTROL OF A CHIMERIC FICOLIN-ANGIOPOIETIN FUSION PROTEIN

Even today, there is frequently no cure for glaucoma, an eye disease. Therefore, research efforts to find new treatments must be accelerated. In many cases, current treatments and surgical methods are not effective, show little success and, frequently, are not well tolerated. Therefore, new treatments for the continuously increasing number of patients suffering from glaucoma are needed – in particular, by ensuring the permanent reduction of intraocular pressure. To achieve this effect, the use of innovative molecules is aimed at stabilizing the vascular endothelium.

This strategy is based on addressing a reversible small molecule inhibitor (vascular endothelial protein tyrosine phosphatase (VE-PTP)). A specifically developed fusion protein with a reinforced modulating effect on the signal path (referred to above) is intended to repair defective Schlemm canals in the eye - which leads to increased liquid flow. As a result, intraocular pressure would be reduced, which would, in principle, cure glaucoma.

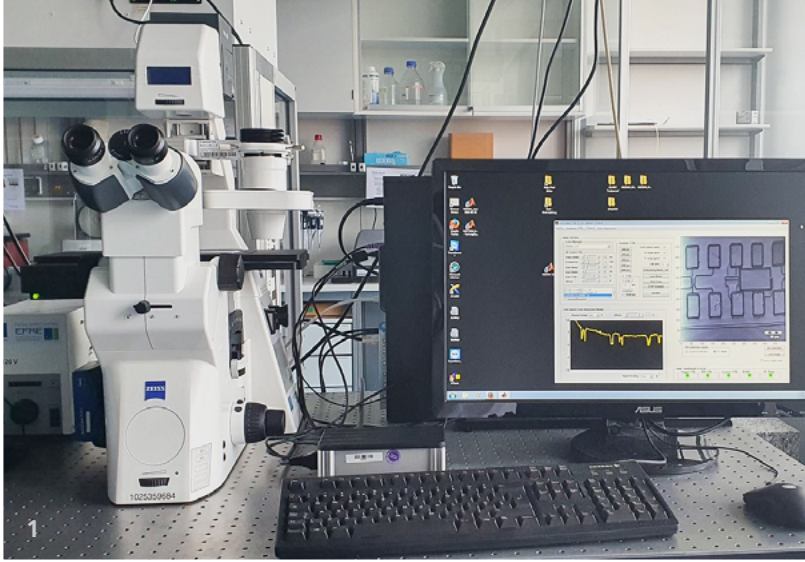
Moreover, this therapeutic principle is to be evaluated in the context of SARS-COV-2 infections. This infection frequently involves damage to the endothelium – particularly in lung tissue. A stabilization of the endothelium would, therefore, be very valuable here as well.

For this reason, this project aims to establish a GMP-compliant production process (in particular as regards cell lines and master cell banks, as well as upstream and downstream process development) for the fusion protein. This includes the necessary quality control at Fraunhofer IZI so as to ensure the efficient and effective clinical application of the biomolecule.

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¹ Homology model of the chimeric recombinant fusion protein Ang1 mimetic.



NON-DESTRUCTIVE TEST AND MEASUREMENT METHODS IN THE BIO-NANOTECHNOLOGY APPLICATION LABORATORY

The Bio-Nanotechnology Application Laboratory (BNAL) in Leipzig is a research infrastructure jointly run by Fraunhofer IZI and Fraunhofer IKTS. With their modern imaging and nanotechnologies, both institutes are opening up new areas of application in biomedicine. State-of-the-art equipment allows biological and medical issues to be handled in an interdisciplinary manner. This means that research and development services can be carried out from fundamental biomedical research through to process development, right over to the development and validation of the latest technologies and system solutions. The combination of biological and medical expertise at Fraunhofer IZI and established analysis methods for material diagnostics at Fraunhofer IKTS paves the way for new diagnostic and therapeutic technologies and procedures.

Non-destructive test and measurement methods for biointerface studies on optically opaque materials are currently being established and evaluated in various projects. The focus is placed here on investigating direct cell-material contact and analyzing material-related effects on the cell adhesion, proliferation and differentiation of different types

of cells using morphological parameters. A modern multi-acousto-scope is being established here as an optical screening tool for cell monitoring and for further cell studies on material surfaces. To this end, the quality and expressiveness of the generated image data are currently being analyzed and optimized for the purpose of cell morphology studies.

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SCIENTIFIC
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Frei gegeben

Gerät: Wave Bioreaktor WAB5

WAB5 qualifiziert am 14.07.
gültig bis 14.07.2025

CONVENTIONS AND CONFERENCES

1. Sächsisches Transferforum,
November 3, 2020, online

**103. Zentrale Fortbildung
Landesapothekerkammer Hessen,**
November 14–15, 2020, online

**11th Annual Symposium Physics of
Cancer,** September 22–24, 2020,
Leipzig, Germany

**12. Jahrestagung der Deutschen
Gesellschaft für Nephrologie
(DGfN),** October 1–4, 2020, Berlin,
Germany

**16th Leipzig Research Festival for
Life Sciences 2020,** January 30, 2020,
Leipzig, Germany

**17. International Symposium on
Amyloidosis ISA,** September 14–18,
2020, online

**17. Jahrestagung des Deutschen
Prostatakarzinom Konsortium e.V.
(DPKK),** January 31 – February 1, 2020,
Dresden, Germany

**18. Wissenschaftliche Tagung der
Sektion Phykologie in der
Deutschen Botanischen Gesell-
schaft,** March 8–11, 2020, Kloster
Steinfeld, Germany

19th Annual Peptalk, January 20–24,
2020, San Diego, USA

2. Tag der Immunforschung,
November 2, 2020, online

2020 BIO International Convention,
June 8–11, 2020, online

**23. biosaxony vor Ort: “Cutting
Edge – Innovationen in der Medizin
durch Zell- und Gentherapeutika”,**
December 1, 2020, online

2nd European CAR T Cell Meeting,
January 30 – February 1, 2020, Sitges,
Spain

**3. Veranstaltung des KI-Hub
Sachsen,** July 1, 2020, Leipzig,
Germany

**33rd International Conference on
Antiviral Research (ICAR),**
September – December 2020, online

34. Deutscher Krebskongress 2020,
February 19–22, 2020, Berlin, Germany

**3rd International Conference on
Zika Virus and Aedes Related
Infections,** February 13–16, 2020,
Washington DC, USA

3rd Snow Algae Meeting (SAM),
November 12, 2020, online

**4. Life-Sciences-Forum Sachsen
2020,** September 9, 2020, online

**4. Ulm Meeting – Biophysics of
Amyloid Formation,** February 18–20,
2020, Ulm, Germany

**46th Annual Meeting of the
European Society for Blood and
Marrow Transplantation,**
August 29 – September 1, 2020, online

4th AMR Conference, August 24–28,
2020, online

4th Global C&D TECH FAIR,
January 29, 2020, Seoul, South Korea

**51. Jahrestagung der Deutschen
Gesellschaft für Medizinische Physik
(e.DGMP),** September 9–11, 2020,
online

**58. Wissenschaftliche Tagung der
Gesellschaft für Versuchstierkunde
GV-SOLAS und 19. Fortbildungs-
veranstaltung der IGTP,** September
16–18, 2020, online

5th German Pharm-Tox Summit,
March 2–5, 2020, Leipzig, Germany

72. Kongress der Deutschen Gesellschaft für Urologie e.V., September 24–26, 2020, online

72nd Annual Meeting of the German Society for Hygiene and Microbiology (DGHM) & Annual Meeting 2020 of the Association for General and Applied Microbiology (VAAM), March 8–11, 2020, Leipzig, Germany

7th Immunotherapy of Cancer Conference ITOC7, October 2–3, 2020, online

Aktuelle Debatten in der 3R-Forschung (ICAR3R), October 1, 2020, online

Analytica, October 19–23, 2020, online

Annual EUROoCS Conference 2020, July 8–9, 2020, online

Bildverarbeitung für die Medizin 2020, March 15–17, 2020, Berlin, Germany

BIO Europe 2020, October 26–29, 2020, online

CeNS Colloquium, January 10, 2020, Munich, Germany

CMCB Life Sciences Seminar 2020, November 26, 2020, online

CMWP Scientific & Educational Meeting (EBMT), January 24–25, 2020, Leipzig, Germany

DELAB-Fachtagung, November 13, 2020, online

Deutsches Wirtschaftsforum Digital, June 29–30, 2020, online

e:Med Kick-off Meeting 2020, November 24–25, 2020, online

Expertenkonferenz zur Systemmedizin, December 15, 2020, online

Formnext Connect, November 10–12, 2020, online

Fraunhofer Solution Days 2020, October 26–29, 2020, online

Fraunhofer Symposium Netzwerk, February 18–19, 2020, Munich, Germany

Genesis 2020, December 10, 2020, online

German R&D Tour – InnoHealth China, December 2–7, 2020, online

IGUS Virtuelle Messe, October 28, 2020, online

Immuno-Oncology 2020, June 3, 2020, online

INC Meets Biosaxony, November 16, 2020, online

INNEO Virtual KeyShot World 2020, July 7, 2020, online

ISCT 2020, May 28–29, 2020, online

ISEV2020 Virtual Meeting, July 20–22, 2020, online

Jahrestagung der Deutschen, Österreichischen und Schweizerischen Gesellschaften für Hämatologie und Medizinische Onkologie 2020, October 9–11, 2020, online

MEDICA 2020, November 16–19, 2020, online

Onkologie im Dialog, September 26, 2020, Lichtenstein/Saxony, Germany

PEGS Europe, November 9–12, 2020, online

Personalised medicine in oncology: Benefits for cancer patients, society and health systems in Germany and Europe (vfa-Veranstaltung),
November 25, 2020, online

Phacilitate Leaders World & World Stem Cell Summit 2020,
January 21–24, 2020, Miami, USA

SARS-CoV-2: Towards a New Era in Infection Research (EMBL Conference), July 3, 2020, online

Science Against SARS-CoV-2 Conference, October 6–8, 2020, online

Simplifying GMP CAR-T and CAR NK cell therapy manufacturing processes, June 9, 2020, online

Targeting antivirals against SARS-CoV-2 (COVID-19) and future zoonotic coronaviruses, February 27, 2020, online

Wago Live SPS, December 1–3, 2020, online

Zoonoses 2020 – International Symposium on Zoonoses Research, October 14–16, 2020, Berlin, Germany

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**Helmholtz-Zentrum Geesthacht,
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Research (HZG)**, Teltow, Germany

**Helmholtz Zentrum München
German Research Center for
Environmental Health**, Munich,
Germany

**Hospital St. Elisabeth and St.
Barbara**, Halle (Saale), Germany

**Hudson Institute of Medical
Research**, Melbourne, Australia

Humboldt-Universität, Berlin,
Germany

**Innovation Center Computer
Assisted Surgery - ICCAS**, Leipzig,
Germany

**Innovations for High Performance
Microelectronics, Leibniz Institute
for Innovative Microelectronics**,
Frankfurt (Oder), Germany

**Institut für Bioprozess- und
Analysenmesstechnik (iba) e.V.**,
Heilbad Heiligenstadt, Germany

**Institut für Dünnschichttechnologie
und Mikrosensorik e.V.**, Teltow,
Germany

**Institute for Applied Informatics
(InfAI)**, Leipzig, Germany

**International Centre of
Biodynamics**, Bukarest, Romania

IRGIB Africa University, Cotonou,
Benin

Jagiellonian University, Krakow,
Poland

**Johannes Gutenberg University
Mainz (JGU)**, Mainz, Germany

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

Karolinska Institutet, Stockholm,
Sweden

KU Leuven, Leuven, Belgium

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

**Leibniz Institute for Zoo and
Wildlife Research (IZW)**, Berlin,
Germany

**Leibniz Institute of Surface
Engineering**, Leipzig, Germany

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

Leipzig Heart Center, Leipzig,
Germany

Leipzig University, Leipzig, Germany

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

**Liverpool School of Tropical
Medicine**, Liverpool, Great Britain

**Ludwig-Maximilians-Universität
München**, Munich, Germany

Mahidol University, Nakhon Pathom,
Thailand

Makerere University, Kampala,
Uganda

**Manipal Academy of Higher
Education**, Manipal, India

**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 of Colloids and
Interfaces**, Potsdam, Germany

**Max Planck Institute of Molecular
Cell Biology and Genetics**, Dresden,
Germany

**Max Planck Institute of Molecular
Plant Physiology**, Potsdam, Germany

McGill University, Montreal, Canada

McMaster University, Hamilton,
Canada

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

MD Anderson Cancer Center,
Houston, USA

Monash University, Melbourne,
Australia

Multitel, Mons, Belgium

**National Autonomous University of
México**, Ciudad de México, México

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

Newcastle University, Newcastle
upon Tyne, Great Britain

**Nikolaus-Fiebiger-Zentrum für
Molekulare Medizin (NFZ)**, Erlangen,
Germany

Nottingham Trent University,
Nottingham, Great Britain

Oslo University Hospital, Oslo,
Norway

Ospedale San Raffaele S.r.l., Milan,
Italy

**Otto von Guericke University
Magdeburg**, Magdeburg, Germany

Paderborn University, Paderborn,
Germany

**Paul Flechsig Institute of
Brain Research**, Leipzig, Germany

**Pilot Pflanzenöltechnologie
Magdeburg e. V. (PPM)**, Magdeburg,
Germany

**Potsdam Institute for Climate
Impact Research**, Potsdam, Germany

REGIOMED-KLINIKEN GmbH,
Coburg, Germany

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

Robert Koch Institute, Berlin,
Germany

Rostock University Medical Center,
Rostock, Germany

Ruhr-Universität Bochum (RUB),
Bochum, Germany

**Rural Service Center of Rhineland-
Palatinate**, Bernkastel, Germany

Saarland University, Homburg,
Germany

**Saxony State Office for the Environ-
ment, Agriculture and Geology**,
Köllitsch, Germany

Seoul National University, Seoul,
South Korea

Städtisches Klinikum "St. Georg"
Leipzig, Leipzig, Germany

**Städtisches Klinikum Braunschweig
gGmbH**, Braunschweig, Germany

**Technical University of Applied
Sciences Wildau**, Wildau, Germany

**Technical University of Munich
(TUM)**, Munich, Germany

Technische Universität Berlin, Berlin,
Germany

**Technische Universität
Braunschweig**, Braunschweig,
Germany

**Technische Universität Dresden
(TUD)**, Dresden, Germany

Tel Aviv University, Tel Aviv, Israel

The University of Edinburgh,
Edinburgh, Great Britain

Thüringer Tierseuchenkasse, Jena,
Germany

Tübingen University Hospital,
Tübingen, Germany

Ulm University, Ulm, Germany

Uniformed Services University,
Bethesda, USA

**Universidade Federal do Rio de
Janeiro – UFRJ**, Rio de Janeiro, Brasil

Université Claude Bernard Lyon 1,
Lyon, France

University Hospital Dresden,
Dresden, Germany

University Hospital Erlangen,
Erlangen, Germany

University Hospital Essen, Essen,
Germany

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

University Hospital of the Saarland,
Homburg / Saar, Germany

University Hospital of Würzburg,
Würzburg, Germany

University Hospital Regensburg,
Regensburg, Germany

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

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

**University of Applied Sciences
Bremerhaven**, Bremerhaven

**University of Applied Sciences
Hannover**, Hannover, Germany

University of Bergen, Bergen, Norway

University of Bern, Bern, Switzerland

University of Bonn, Bonn, Germany

University of California, San Diego /
Los Angeles, USA

University of Cambridge, Cambridge,
Great Britain

University of Cologne, Cologne,
Germany

University of Freiburg, Freiburg,
Germany

University of Glasgow, Glasgow,
Great Britain

University of Graz, Graz, Austria

University of Greifswald, Greifswald,
Germany

University of Innsbruck, Innsbruck,
Austria

University of Zurich, Zurich,
Switzerland

University of Kassel, Kassel, Germany

Uppsala University, Uppsala, Sweden

**University of Leipzig Medical
Center**, Leipzig, Germany

**Washington University School of
Medicine**, St. Louis, USA

**University of Massachusetts
Amherst**, Amherst, USA

University of Münster, Münster,
Germany

University of Padua, Padua, Italy

University of Potsdam, Potsdam,
Germany

University of Rostock, Rostock,
Germany

University of Salzburg, Salzburg,
Austria

**University of Veterinary Medicine
Hannover, Foundation**, BÜsum,
Germany

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AESKU.GROUP GmbH, Wendelsheim, Germany

Afex GmbH, Mildenau, Germany

Affimed GmbH, Heidelberg, Germany

AiCuris GmbH & Co. KG, Wuppertal, Germany

AIM - Advanced Identification Methods GmbH, Leipzig, Germany

Airbus AG, Hamburg, Germany

AJ Roboscreen GmbH, Jena, Germany

AKT Angewandte Kommunikationstechnik GmbH, Beucha, Germany

Albutec GmbH, Rostock, Germany

alphaomega Labor GbR, Leipzig, Germany

ALS Automated Lab Solutions GmbH, Jena, Germany

AnaPath Services GmbH, Liestal, Switzerland

aokin AG, Berlin, Germany

AptaIT GmbH, Munich, Germany

Artcline GmbH, Rostock, Germany

Asahi Kasei Corp., Tokyo, Japan

AVOR AG, Hamburg, Germany

Badische Staatsbrauerei Rothaus AG, Grafenhausen-Rothaus, Germany

BASF SE, Ludwigshafen, Germany

Bausch+Ströbel Maschinenfabrik Ilshofen GmbH+Co. KG, Ilshofen, Germany

Becit GmbH, Bitterfeld-Wolfen, Germany

Beiersdorf AG, Hamburg, Germany

BELANO medical AG, Hennigsdorf, Germany

BellaSeno GmbH, Leipzig, Germany

Berthold Technologies GmbH & Co. KG, Bad Wildbad, Germany

BianoGMP GmbH, Gera, Germany

BianoScience GmbH, Zwickau, Germany

BiFlow Systems GmbH, Chemnitz, Germany

Bill and Melinda Gates Foundation, Seattle, USA

BioArtProducts GmbH, Rostock, Germany

BioComo Incorporation, Komono, Japan

BioCopy GmbH, Freiburg im Breisgau, Germany

BIOCYC Gesellschaft für Biotechnologie und Recyclingverfahren mbH & Co. Entwicklungs KG, Potsdam, Germany

BioEcho Life Sciences GmbH, Dormagen, Germany

BioGenes GmbH, Berlin, Germany

BioPlanta GmbH, Grimma, Germany

BioScientia Sp. z o.o., Poznań, Poland

BIOSYNTAN GmbH, Berlin, Germany

BioTeZ Berlin Buch GmbH , Berlin, Germany	Cogen Therapeutics , Cambridge, MA, USA	Epimune GmbH , Berlin, Germany
BM Bioscience Technology GmbH , Laage, Germany	Colibri Photonics GmbH , Potsdam, Germany	epiontis GmbH , Berlin, Germany
BMG LABTECH GmbH , Ortenberg, Germany	ConsulTech GmbH , Berlin, Germany	Epitopic GmbH , Leipzig, Germany
Boehringer Ingelheim Veterinary Research Center GmbH&Co.KG , Hannover, Germany	CureVac AG , Tübingen, Germany	ERBER AG , Getzersdorf, Austria
Brandenburg Antiinfektiva GmbH , Borstel, Germany	CytoSorbents Europe GmbH , Berlin, Germany	ERT-OPTIK Dr. Thiel GmbH , Ludwigshafen, Germany
CANDOR Bioscience GmbH , Wangen, Germany	Daiichi Sankyo Co., Ltd. , Tokyo, Japan	Erwin Quader Systemtechnik GmbH , Espelkamp, Germany
Cellavent GmbH , Düsseldorf, Germany	Dermatest GmbH , Münster, Germany	Evonik Creavis GmbH , Marl, Germany
cellerata GmbH , Ulm, Germany	diamond inventics GmbH , Berlin, Germany	Fassisi, Gesellschaft für Veterinär-diagnostik und Umweltanalysen mbH , Göttingen, Germany
Chembio Diagnostics GmbH , Berlin, Germany	DMCE GmbH & Co KG , Linz, Austria	FIM Biotech GmbH , Berlin, Germany
Chimera Biotec GmbH , Dortmund, Germany	DST – Diagnostische Systeme & Technologien GmbH , Schwerin, Germany	Fresenius Kabi Deutschland GmbH , Bad Homburg, Germany
Clearum GmbH , Rostock, Germany	DYN Labs Ltd. , Caesarea, Israel	Fresenius Medical Care AG & Co. KGaA , Bad Homburg, Germany
C-Lecta GmbH , Leipzig, Germany	ECH Elektrochemie Halle GmbH , Halle (Saale), Germany	fzmb GmbH , Bad Langensalza, Germany
CO.DON AG , Teltow, Germany	Ella Biotech Gesellschaft für angewandte Biotechnologie mbH , Munich, Germany	GCI GmbH , Köings Wusterhausen, Germany

Genevention GmbH, Göttingen,
Germany

**Geräte- und Vorrichtungsbau
Spitzner OHG**, Leipzig, Germany

**GeSiM Gesellschaft fuer Silizium-
Mikrosysteme mbH**, Großberkmannsdorf,
Germany

GlyProVac ApS., Odense, Denmark

GNA Biosolutions GmbH, Martinsried,
Germany

GVG Diagnostics GmbH, Leipzig,
Germany

IBA GmbH, Göttingen, Germany

Ichor Medical Systems, Inc., San
Diego, USA

Icon Genetics GmbH, Halle (Saale),
Germany

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

Idris Oncology, Leiden,
The Netherlands

IgNova GmbH, Oberursel, Germany

Immunic AG, Martinsried, Germany

Immunolab GmbH, Kassel, Germany

ImReg Pharmaceuticals GmbH,
Leipzig, Germany

in.vent DIAGNOSTICA GMBH,
Hennigsdorf, Germany

Innovative Molecules GmbH,
Bad-Salzuflen, Germany

**inotec Forschungs- und
Entwicklungsgesellschaft mbH**,
Leipzig, Germany

Institut für Produktqualität GmbH,
Berlin, Germany

InstrAction GmbH, Mannheim,
Germany

INVICOL GmbH, Berlin, Germany

InVivo BioTech Services GmbH,
Hennigsdorf, Germany

Iovance Biotherapeutics Inc, San
Carlos, USA

Ipratech SA, Mons, Belgium

Kapelan Bio-Imaging GmbH, Leipzig,
Germany

Katz Biotech AG, Baruth, Germany

Kephera Diagnostics, LLC,
Framingham, USA

**KET Kunststoff- und Elasttechnik
GmbH**, Radeberg, Germany

Life Science Inkubator GmbH, Bonn,
Germany

Lipocalyx GmbH, Halle (Saale),
Germany

LOHMANN TIERZUCHT GmbH,
Cuxhaven, Germany

**LSA GmbH Leischnig Schaltschrank-
bau Automatisierungstechnik**,
Wolkenstein, Germany

Lufthansa Technik AG, Hamburg,
Germany

LXP Group GmbH, Teltow, Germany

M2-Automation GmbH, Berlin,
Germany

Magna Diagnostics GmbH, Leipzig,
Germany

Mannin GmbH, Leipzig, Germany

Medichema GmbH, Chemnitz,
Germany

MEDIPAN GmbH, Blankenfelde-Mahlow, Germany

Mibelle Biochemistry, Mibelle AG, Buchs, Switzerland

micro resist technology Gesellschaft für chemische Materialien spezieller Photoresistsysteme mbH, Berlin, Germany

MicroDiscovery GmbH, Berlin, Germany

microfluidic ChipShop GmbH, Jena, Germany

MicroMatrices Associates Ltd, Dundee, Great Britain

MIKROGEN GmbH, Neuried, Germany

Molzymb GmbH & Co. KG, Bremen, Germany

nal von minden GmbH, Regensburg, Germany

Navigo Proteins GmbH, Halle (Saale), Germany

new/era/mabs, Potsdam, Germany

Nipro Europe NV, Brussels, Belgium

Nomad Bioscience GmbH, Halle (Saale), Germany

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

NovaTec Immundiagnostica GmbH, Dietzenbach, Germany

Novidi GmbH, Hamburg, Germany

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

opTricon – Entwicklungsgesellschaft für Optische Technologien mbH, Berlin, Germany

PAN-Biotech GmbH, Aidenbach, Germany

PerioTrap Pharmaceuticals GmbH, Halle (Saale), Germany

Plexense, Inc., Gyeonggi-do, South Korea

PolyAn GmbH, Berlin, Germany

PolyQuant GmbH, Bad Abbach, Germany

Praxis Pharmaceutical S.A.U., Vitoria-Gasteiz, Spain

Primacyt GmbH, Schwerin, Germany

Primedica GmbH, Dortmund, Germany

Protinhi Therapeutics B.V., Nijmegen, The Netherlands

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

Roboscreen GmbH, Leipzig, Germany

Roche Glycart AG, Schlieren, Switzerland

SanWa Biotech, Hong Kong, China

Sartorius Stedim Biotech GmbH, Göttingen, Germany

SB Science Management UG, Berlin, Germany

SCHMUHL Faserverbundtechnik GmbH & Co. KG, Remptendorf, Germany

Scienion AG, Berlin / Dortmund, Germany

scienova GmbH, Jena, Germany

selectION Therapeutics GmbH,
Martinsried, Germany

SELEKTIS GmbH, Berlin, Germany

SelfDiagnostics Deutschland GmbH,
Leipzig, Germany

Seramun Diagnostica GmbH,
Heidesee, Germany

Serumwerk Bernburg AG, Bernburg,
Germany

SerYmun Yeast GmbH, Halle (Saale),
Germany

SFC Co., Ltd., Yongin /
Chungcheonbuk-do, South Korea

Siemens AG, Munich / Erlangen,
Germany

Siemens Healthcare Laboratory, LLC,
Berkeley, USA

SinapTec Ultrasonic, Lezennes, France

**SKW Stickstoffwerke Piesteritz
GmbH,** Lutherstadt Wittenberg,
Germany

Sonovum GmbH, Leipzig, Germany

Surflay Nanotec GmbH, Berlin,
Germany

TBioMed, Heinrichsberg, Germany

Tcell Tolerance GmbH, Leipzig,
Germany

TIB MOLBIOL Syntheselabor GmbH,
Berlin, Germany

Trifolio-M GmbH, Lahnau, Germany

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

UP Transfer GmbH, Potsdam,
Germany

Villeroy & Boch AG, Mettlach,
Germany

Vita34 AG, Leipzig, Germany

Vivoryon Therapeutics AG, Halle
(Saale), 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

Instrumental analytics (training / lecture / seminar), Prof. Dr. Stephan Schilling

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

COBURG UNIVERSITY OF APPLIED SCIENCES AND ARTS

Biochemistry – signal pathways (lecture), Prof. Dr. Stefan Kalkhof

Chromatography (lecture), Prof. Dr. Stefan Kalkhof

Instrumental analytics (problem-oriented learning), Prof. Dr. Stefan Kalkhof

Molecular spectroscopy (lecture), Prof. Dr. Stefan Kalkhof

New trends clinical analytics (problem-oriented learning), Prof. Dr. Stefan Kalkhof

Protein analytics (lecture), Prof. Dr. Stefan Kalkhof

Protein / ligand modelling (problem-oriented learning), Prof. Dr. Stefan Kalkhof

Protein mass spectrometry (problem-oriented learning), Prof. Dr. Stefan Kalkhof

DHIRUBHAI AMBANI INSTITUTE OF INFORMATION AND COMMUNICATION TECHNOLOGY

Smart Molecules and Self-assembly (lecture), Dr. David M Smith

GESELLSCHAFT DEUTSCHER CHEMIKER (GDCH)

Application of modern HPLC (course), Prof. Dr. Stefan Kalkhof

LEIPZIG UNIVERSITY

Animal models in preclinical development (lecture), Claudia Müller

Cellular immunotherapy (MSc Clinical Research) (lecture), Prof. Dr. Dr. Ulrike Köhl

Fundamentals of Good Laboratory Practice – GLP (lecture), Dr. Jörg Lehmann

Fundamentals of pharmaceutical chemistry including nomenclature, analytics and toxicology of organic drugs, excipients and pollutants (training), Dr. Daniel Ramsbeck

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

Molecular nanotechnology (seminar), Dr. David M Smith

Molecular oncology and immunology (lecture), Prof. Dr. Friedemann Horn

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

Pharmaceutical chemistry (seminar),

Dr. Mirko Buchholz

Preclinical in vitro and in vivo models for the detection and evaluation of immunotoxic effects of drugs (lecture),

Sina Riemschneider

QSB4 autoimmunity and pathogenic immune reactions (seminar), Dr. Peter Ruschpler**Soft matter physics and biological physics (lecture / seminar),**

Dr. Jörg Schnauß

Soft matter physics and biological physics (seminar), Dr. David M Smith**Statistical learning (lecture),**

Dr. Kristin Reiche, Dr. David Petroff, Dr. Andreas Kühnapfel, Prof. Martin Bogdan

Theory and practice HPLC (course),

Prof. Dr. Stefan Kalkhof

Tumor immunology (QSB4 – 10th semester) (lecture),

Prof. Dr. Dr. Ulrike Köhl

Vector-borne virus infection**(lecture),** PD Dr. Sebastian Ulbert**Virology (training),** Dr. Lea Bayer,

PD Dr. Thomas Grunwald

LEIPZIG UNIVERSITY OF APPLIED SCIENCES (HTWK LEIPZIG)**Biomedical imaging (lecture),**

Dr. Sebastian Greiser

Biomedical imaging (lecture),

Prof. Dr. Ulf-Dietrich Braumann

Biomedical information technology**(seminar),** Prof. Dr. Ulf-Dietrich Braumann**Image processing (lecture),**

Prof. Dr. Ulf-Dietrich Braumann

Imaging (training),

Prof. Dr. Ulf-Dietrich Braumann

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

Dr. Sebastian Greiser

Microscopic imaging (lecture), Prof.

Dr. Ulf-Dietrich Braumann

MARTIN LUTHER UNIVERSITY**HALLE-WITTENBERG****Lab Course on Vector Construction****(training),** Prof. Dr. Stephan Schilling**Molecular Biotechnology:****Construction of Hosts and Vectors****(lecture),** Prof. Dr. Stephan Schilling**non-curricular teaching (module supervision biochemistry / molecular biology for physicians and dentists) (seminar / training),**

Dr. Holger Cynis

ZITTAU-GÖRLITZ UNIVERSITY OF APPLIED SCIENCES**Xenotransplantation (lecture),**

Dr. Anke Hoffmann

EVALUATOR ACTIVITIES

Acta Neuropathologica,
Prof. Dr. Stephan Schilling

Alzheimer's Association,
Dr. Holger Cynis

**Applications for Deutsche
Krebshilfe,** Prof. Dr. Dr. Ulrike Köhl

**Applications for Humboldt
Foundation,** Prof. Dr. Dr. Ulrike Köhl

**Applications of Young Scientists of
Leipzig University,**
Prof. Dr. Dr. Ulrike Köhl

Biomacromolecules,
Dr. David M Smith

**BMC Bioinformatics (Associate
Editor),** Dr. Kristin Reiche

Bundesgesundheitsblatt,
Dr. Jörg Lehmann

Cancer Research, Dr. Holger Cynis

Cancers, Dr. Jörg Lehmann

Charite Berlin Professor,
Prof. Dr. Dr. Ulrike Köhl

ChemistryOpen (Journal),
Dr. Daniel Ramsbeck

ChemistrySelect (Journal),
Dr. Daniel Ramsbeck

ChemMedChem (Journal),
Dr. Daniel Ramsbeck

Clinical Science, Dr. Jörg Lehmann

**Cluster application RCI Regensburg
Center for Interventional
Immunology,** Prof. Dr. Dr. Ulrike Köhl

Cytometry Part A (Editor-in-Chief),
Prof. Dr. Attila Tárnok

**Developmental and Comparative
Immunology,** Dr. Jörg Lehmann

**DFG project review "Digital twin-
supported process design for NK
cell therapies",** Prof. Dr. Dr. Ulrike Köhl

Emerging Microbes and Infection,
PD Dr. Sebastian Ulbert

European Journal of Immunology,
PD Dr. Thomas Grunwald

Expert Opinion On Drug Safety,
Dr. Jörg Lehmann

Faculty Opinions (F1000),
Dr. Jörg Lehmann

**French National Cancer Institute,
program PRT-K2020, project review
"Generating non-genetically
modified CAR-like NK cells",**
Prof. Dr. Dr. Ulrike Köhl

**Frontiers Immunology (Editorial
Board),** Prof. Dr. Dr. Ulrike Köhl

Future Virology, PD Dr. Sebastian
Ulbert

**Gamma Delta Therapeutics London
(Scientific Advisory Board),**
Prof. Dr. Dr. Ulrike Köhl

Helmholtz cluster application,
Prof. Dr. Dr. Ulrike Köhl

Helmholtz Association,
PD Dr. Thomas Grunwald

**International Journal of
Environmental Research and Public
Health (MDPI) (Editorial Board),**
Dr. Jörg Lehmann

**Journal of Clinical Cancer Research
(Editorial Board),**
Prof. Dr. Dr. Ulrike Köhl

Journal of Medicinal Chemistry,
Dr. Daniel Ramsbeck

Journal of Proteomics,

Prof. Dr. Stefan Kalkhof

Leibniz application,

Prof. Dr. Dr. Ulrike Köhl

Mol Biol Rep, Dr. Holger Cynis**Molecular Biology Reports,**

PD Dr. Sebastian Ulbert

Molecules, Prof. Dr. Stephan Schilling**Nanoscale,** Dr. David M Smith**Pharmaceuticals (Journal),**

Dr. Daniel Ramsbeck

Pharmaceutics, PD Dr. Sebastian Ulbert**PLoS ONE,** Dr. Jörg Lehmann**Research proposals Deutsche
Forschungsgemeinschaft (DFG,
German Research Foundation),**

Dr. Thomas Leya

Review Journals - Clinical**Pharmacology & Therapeutics,
Nature Medicine, Gene Therapy,
Transfusion Medicine,**

Prof. Dr. Dr. Ulrike Köhl

Scientific Reports, Prof. Dr. StefanKalkhof, Dr. Gustavo Makert dos
Santos, PD Dr. Sebastian Ulbert**SPIE Medical Imaging: Digital and
Computational Pathology
Conference,**

Prof. Dr. Ulf-Dietrich Braumann

Ticks and tick borne diseases,

PD Dr. Sebastian Ulbert

**University of Duisburg-Essen (UDE),
W2 – Pediatric stem cell therapy,**

Prof. Dr. Dr. Ulrike Köhl

Vaccine, PD Dr. Thomas Grunwald**Vaccines,** PD Dr. Thomas Grunwald**Veterinary Immunology and
Immunopathology,** Dr. Jörg Lehmann**Viruses,** Dr. Holger Cynis, PD Dr.Thomas Grunwald, PD Dr. Sebastian
Ulbert

ASSOCIATION MEMBERSHIPS

ACS (American Chemical Society),

Dr. Daniel Ramsbeck

Alliance for Regenerative Medicine,

Dr. Thomas Tradler, MBA, Fraunhofer IZI

Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment

(ISTAART), Dr. Holger Cynis,

Prof. Dr. Stephan Schilling

American Chemical Society (ACS),

Dr. Daniel Ramsbeck,

Dr. Mirko Buchholz

American Society for Mass

Spectrometry, Prof. Dr. Stefan Kalkhof

bbb – Biotechnologieverbund

Berlin-Brandenburg e.V.,

Dr. Thomas Tradler MBA

biosaxony e. V., Dr. Thomas Tradler

MBA, Fraunhofer IZI

btS - Life Sciences Studierenden- initiative e.V., Carolin Meier

Dachverband der Technologen/ -innen und Analytiker/-innen in der Medizin Deutschland e.V.,

Ulrike Ehlert

DECHEMA - Gesellschaft für Chemische Technik und Biotechnologie e.V. (Society for Chemical Engineering and Biotechnology), Dr. Mirko Buchholz

Deutsch-Kanadische Gesellschaft (DKG), Dr. Thomas Tradler MBA

Deutsche Arbeitsgemeinschaft für Knochenmark und Blutstammzell- transplantation e.V. (DAG-KBT),

Prof. Dr. Dr. Ulrike Köhl

Deutsche Gesellschaft für Allergologie und Klinische Immunologie (DGAKI) e.V.,

Dr. Elke Ueberham

Deutsche Gesellschaft für experimentelle und klinische Pharmakologie und Toxikologie e.V. (DGPT), Dr. Jörg Lehmann

Deutsche Gesellschaft für Gentherapie e.V. (DG-GT),

Prof. Dr. Dr. Ulrike Köhl

Deutsche Gesellschaft für Geschichte der Pharmazie (DGGP),

Dr. Mirko Buchholz

Deutsche Gesellschaft für Hämatologie und Medizinische Onkologie e.V. (DGHO),

Prof. Dr. Dr. Ulrike Köhl

Deutsche Gesellschaft für Medizinische Physik e.V.,

Prof. Dr. Ulf-Dietrich Braumann

Deutsche Gesellschaft für Parasitologie (DGP),

Dr. Markus von Nickisch-Roseneck

Deutsche Gesellschaft für Pathologie e.V., Dr. Kristin Reiche

Deutsche Gesellschaft für Regenerative Medizin e.V.,

Fraunhofer IZI

Deutsche Nucleinsäurechemie- gemeinschaft e.V. (DNG),

Dr. Marcus Menger

Deutsche Pharmazeutische Gesellschaft e.V., Sebastian Beck,

Dr. Mirko Buchholz, Dr. Daniel

Ramsbeck, Dr. Julia Stäker

DFG Cluster of Excellence "Rebirth – Regenerative Medicine",

Prof. Dr. Dr. Ulrike Köhl

DiagnostikNet-BB e. V. Netzwerk Diagnostik Berlin-Brandenburg,
Dr. Marcus Menger

DIN-Normenausschuss Grundlagen des Umweltschutzes (NAGUS) – NA 172-00-16 AA Arbeitsausschuss Algen und Algenprodukte,
Dr. Thomas Leya

European Academy of Allergy and Clinical Immunology (EAACI),
Lisbeth Ramirez Caballero

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

European Society for Medical Oncology (ESMO),
Prof. Dr. Dr. Ulrike Köhl

European Society for Virology (ESV),
Dr. Jasmin Fertey, PD Dr. Sebastian Ulbert

Freundeskreis Tiermedizin der Veterinärmedizinischen Fakultät Leipzig e.V., Dr. Anke Hoffmann,
Dr. Jörg Lehmann

German Cancer Society,
Dr. Kristin Reiche

German Lymphoma Alliance e.V.,
Dr. Markus Kreuz

German Physical Society, Tina Händler, PD Dr. Ralph Hölzel, Dr. Jörg Schnaus

German Qualified Person Association (GQPA), Ulrike Jehmlich,
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ABSTRACTS

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Köhl U. **Gegenwart und Zukunft lebender Krebsmedikamente - Made in Sachsen.** Onkologie im Dialog, September 26, 2020, Lichtenstein / Saxony, Germany

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Köhl U. **In vivo therapy trials of CAR NK-based ATMPs redirected against head and neck cancer - proof of concept.** TIMER-2020-Meeting, September 13–14, 2020, virtual

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Menger M. **Aptamers as specific recognition elements.** Kolloquium BTU Sentfenberg, February 5, 2020, Senftenberg, Germany

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Smith D. **Enhancement of bioactive molecules with DNA-templated oligovalence.** CeNS Colloquium, January 10, 2020, Munich, Germany

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Uhlig K. **Organ-on-chip systems that optimise therapeutic strategies for cancer patients.** Fraunhofer Solution Days 2020, October 28, 2020, virtual

Uhlig K. **HepatoTox: in-vitro Hochdurchsatz-Testverfahren zur Bewertung der Lebertoxizität von chemischen Stoffen.** Workshop "FuE Bedarf und regulatorische Aspekte bei Alternativmethoden zum Tierversuch", January 16, 2020, Stuttgart, Germany

Wüstenhagen D. **Cell-Free Synthesis of Proteins.** Kolloquium BTU Sentfenberg, February 5, 2020, Sentfenberg, Germany

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Tárnok A. **Machine learning, COVID-19 (2019-nCoV), and multi-OMICS (Editorial).** Cytometry Part A 97 (2020) 3, pages 215-216. doi: 10.1002/cyto.a.23990

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GRADUATION (CLASS OF 2020)

Alban, Maike. **Entwicklung eines Verfahrens zur Bestimmung des Acetongehaltes in Urinproben mittels SPME-GC-FAIMS.** Coburg University of Applied Sciences and Arts, Bachelor thesis

Altattan, Basma. **Synthesis and Characterization of Functionalized Nanostructures for the Inhibition of Respiratory Syncytial Virus (RSV).** Martin Luther University Halle-Wittenberg, Master thesis

Bauer, Markus. **Entwurf und Validierung unüberwachter Lernmethoden anhand des Prostata-Adenokarzinoms.** Leipzig University of Applied Sciences (HTWK Leipzig), Master thesis

Ferraz, Catarina. **DR5 Stimulation with DNA-templated Multivalent Arrangements of TRAIL-mimicking Peptides.** Leipzig University, Master thesis

Geringswald, Linda. **Heterologe Expression, Reinigung und Charakterisierung des Amyloidpeptids Adan.** Martin Luther University Halle-Wittenberg, Master thesis

Grunwald, Thomas. **Entwicklung neuartiger Impfstoffe gegen das Respiratorische Synzytial-Virus.** Leipzig University, Habilitation

Haenelt, Sarah. **Entwicklung eines Nachweisverfahrens zur Frühdiagnose von Alzheimer mittels Tau-Proteinen.** Saarland University, Master thesis

Helm, Alexandra. **Fluoreszenz-Quenching Assay zum Nachweis von Influenza-Viren.** University of Potsdam, Master thesis

Hensel, Anna-Katharina. **Isothermale Amplifikation von Multiresistenzgenen von Carbapenemen mittels RPA und Detektion durch Hybridisierung auf einem Mikroarray.** University of Potsdam, Bachelor thesis

Jahn, Lucas. **Ansteuerung eines elektrisch beheizbaren und mit thermoresponsiven Polymeren beschichteten Zellkultursubstrates zur Kontrolle neuronalen Zellwachstums.** Technische Universität Berlin, Bachelor thesis

Joas, Maximilian. **Applying Machine Learning Methods for Transcriptome Based Risk Assessment of Prostate Cancer.** Leipzig University, Master thesis

Kern, Karolin. **Identifizierung potentiell allergener Soja-Epitope mittels Peptid Phage Display.** Friedrich-Schiller-Universität Jena, Doctoral thesis

Kristmann, Jenny. **The influence of albumin on transmembrane transport of active substances in human cell lines.** University of Rostock, Bachelor thesis

Lange, Lena. **Analyse eines potentiellen therapeutischen Biomarkers für eine Antikörperbasierte Therapie gegen das dreifach negative Mammakarzinom anhand von Zelllinien und Patientenmaterial.** Technische Universität Dresden (TUD), Bachelor thesis

Le, Thi Thanh Ha. **Immunhistochemische Charakterisierung der lokalen intestinalen Immunantwort im Mausmodell der chronischen bakteriell-induzierten Kolitis.** Leipzig University, Diploma thesis

Leonhardt, Clara. **Immunhistochemische Charakterisierung tumorinfiltrierender Immunzellen im TNBC-Xenotransplantationsmodell in der humanisierten NSG-Maus.** Leipzig University, Diploma thesis

Lott, Jana. **Fluoreszierende Polymernanopartikel als sensitives Detektionssystem - Anwendung am Beispiel eines CRP-Immunoassay.** Coburg University of Applied Sciences and Arts, Bachelor thesis

March, Arianna. **Establishing a microfluidic ELISA assay to detect amyloid- β as early biomarker for Alzheimer's disease.** Rhine-Waal University of Applied Sciences, Bachelor thesis

Mattig, Emily. **Industrieprojekt - Titel unter Geheimhaltung.** University of Potsdam, Master thesis

Nemack, Eric. **Charakterisierung einer mit Mikroheizungen verbundenen thermoresponsiven Zellkulturoberfläche zur örtlichen und zeitlichen Kontrolle neuronalen Zellwachstums.** Technische Universität Berlin, Master thesis

Nieft, Ulrike. **Detektion der Verbreitung extrazellulärer Vesikel im Gewebe mittels bildgebender Analyseverfahren.** Freie Universität Berlin, Bachelor thesis

Panagiotidis, Eleftherios. **Untersuchung der Plasmaproteinbindung von Wirkstoffkandidaten mittels vier verschiedener Analysetechniken.** Aalen University, Master thesis

Petersohn, Clara. **Untersuchung des Einflusses von Mikroplastik auf die transkriptionelle Aktivität von CREB.** Beuth University of Applied Sciences Berlin, Bachelor thesis

Pfennig, Christian. **Vergleichende Untersuchung der Hemmeigenschaften neuartiger Inhibitoren von Meprienen aus Mensch und Maus.** Anhalt University of Applied Sciences, Bachelor thesis

Reißhauer, Susann. **Vergleich zweier Konzepte zur automatisierten Pathogeninaktivierung mittels niederenergetischer Elektronenstrahlung.** Technische Universität Braunschweig, Master thesis

Schaber, Carina. **Analyse der In-vitro-Translationseffizienz von Anti-CD4-CAR-EGFP-mRNA im zellfreien und zellbasierten System.** Coburg University of Applied Sciences and Arts, Bachelor thesis

Schnapp, Lena. **Führungskräfteentwicklung am Fraunhofer IZI Leipzig - Analyse des Personalentwicklungskonzepts für Nachwuchsführungskräfte.** Leipzig University, Master thesis

Schneider, Lukas. **Atemluftanalyse mittels Ionenmobilitätsspektrometrie bei akut COVID-19 Erkrankten und Rekonvaleszenten.** Coburg University of Applied Sciences and Arts, Bachelor thesis

Scholz, Marina. **Integriertes Detektionssystem für biologische Kontaminationen in Treibstoffen.** Beuth University of Applied Sciences Berlin, Master thesis

Schönberg, Alwin. **Konzeption einer variablen Zoomoptik für ein Lichtblattmikroskop.** Aalen University, Bachelor thesis

Schreiber, Tim Heiko. **Immunhistochemische Charakterisierung von Interferon-gamma- und Interleukin-17-produzierenden Immunzellen in der bakteriell-induzierten Kolitis der Maus.** Leipzig University, Diploma thesis

Seeber, Lisa-Marie. **Einfluss von niederenergetischer Elektronenbestrahlung auf die Genexpression und das Wachstum humaner Leukozyten-Linien.** Coburg University of Applied Sciences and Arts, Master thesis

Seier, Florian. **Integration of Synthetic Glycans into Rationally-designed DNA Nanostructures for Capturing Pathogenic Bacteria.** Mittweida University of Applied Sciences, Master thesis

Selke, Jana. **Epitop-Mapping von Serumantikörpern gegen das Dengue-Virus 2 Hüllprotein.** Mittweida University of Applied Sciences, Bachelor thesis

Tame, Anna-Lena. **Immunhistochemische Charakterisierung von folliculären dendritischen Zellen in der humanisierten NSG-Maus.** Coburg University of Applied Sciences and Arts, Master thesis

Vu, My. **Optimization of Throughput, Robustness and Biocompatibility of a Microfluidic Cell Sorting Process Based on Dielectrophoresis.** Technische Universität Berlin, Bachelor thesis

Vu, Tuan Anh. **Entwicklung eines Konzeptes zur Optimierung der Instandhaltung beim Fraunhofer IZI Leipzig für einen ausfallsicheren, effizienten und transparenten Gebäudebetrieb mit Unterstützung eines CAFM Programms.** Leipzig University of Applied Sciences (HTWK Leipzig), Master thesis

Walther, Jenny. **Volumetrische Analyse von Medulloblastom-Strukturen in ausgewählten T2-Kontrastverfahren der Magnetresonanztomografie und Korrelation mit Parametern der Biolumineszenz-Bildgebung im Mausmodell.** University of Applied Sciences Zwickau, Bachelor thesis

Wiltzsch, Vivien. **Identification of the ligand-dependent interactome of the aryl hydrocarbon receptor in murine bone marrow-derived macrophages by affinity-purification mass spectrometry.** Leipzig University, Master thesis

PRIZES

Fraunhofer IZI publications prizes

were awarded to Dr. Karolin Kern on the topic "The immunome of soybean allergy: Comprehensive identification and characterization of epitopes" / to Dr. Alexandra Rockstroh on the topic "Specific Detection and Differentiation of Tick-Borne Encephalitis and West Nile Virus Induced IgG Antibodies in Humans and Horses" / to Christoph Kämpf on the topic "Uap: Reproducible and Robust HTS Data Analysis"

Prize of the sponsoring association of Leipzig University of Applied Sciences (HTWK Leipzig)

was awarded to Georg Popp for his master thesis written at Fraunhofer IZI on the topic "Development of an efficient real-time image fusion algorithm."

PATENTS

The patent portfolio of the Fraunhofer IZI currently holds 47* 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

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

* without Fraunhofer IZI-BB patents



FURTHERANCE

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

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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

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