Fraunhofer IZI

Fraunhofer Institute for Cell Therapy and Immunology IZI

20 YEARS FRAUNHOFER IZI

Annual report 2024/2025

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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 units 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 controls 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.

»Developing the medicine of the future together.«

Organization

You can find a detailed organization chart on our website.

Director

Administration

Executive departments and central facilities / officers

Department of GMP Cell and Gene Therapy

Department of Cell and Gene Therapy Development and Clinical Gene Transfer

Department of Medical Bioinformatics

Department of Infection Research and Diagnostics

Department of Preclinical Development and Validation

Department of Extracorporeal Therapy Systems

Rostock

Department of Drug Design and Target Validation

Halle (Saale)

Department of Cellular Immunotherapy

Würzburg

Branch Bioanalytics and Bioprocesses

Potsdam-Golm

March 1, 2025

Business units and competencies

Cell and gene therapy | Drugs and vaccines | Molecular and immunodiagnostics | Extracorporeal therapies

Drugs & target discovery	Therapy & diagnosis concept	Preclinic & validation	Manufacturing	Clinical trials	Approval
▪ Biomarkers ▪ OMICS platforms (genome, RNA, proteome) ▪ Bioinformatics ▪ Cell analytics	▪ In vitro studies ▪ Bioanalytics ▪ Pharmacology ▪ Vaccines ▪ Antibodies ▪ ATMPs ▪ Small molecules	▪ In vivo studies ▪ GLP testing ▪ Toxicology	▪ Process development ▪ Process validation ▪ Manufacturing authorization ▪ GMP manufacturing	▪ Quality management ▪ Companion diagnostics	▪ Regulatory expertise from preclinic through to approval

Research infrastructure at the Leipzig site

- GMP facilities (1)
- S3 laboratory (2)
- Transparent prototyping laboratory (3)
- Isotope laboratory (4)
- Center for Experimental Medicine (5)
- Seminar area and cafeteria (6)

Buildings

Main building
- Usable area: 4 131 m²
- Lab space: 1 867 m²
- Offices: 1 615 m²
- Seminar area: 276 m²

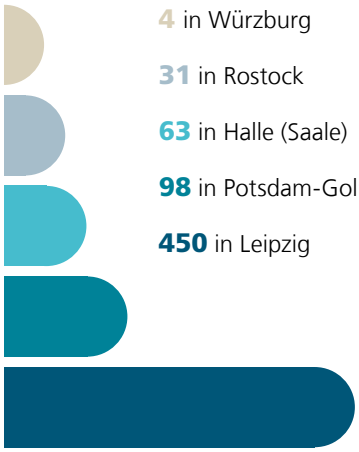
First extension building
- Usable area: 1 568 m²
- Lab space: 470 m²
- Offices: 142 m²
- Clean rooms: 410 m²

Second extension building
- Usable area: 3 050 m²
- Lab space: 1 171 m²
- Offices: 881 m²
- Clean rooms: 402 m²

Rental area at BIO CITY Leipzig
- Clean rooms: 334 m²

Key institute figures 2024

646 employees



4 in Würzburg

31 in Rostock

63 in Halle (Saale)

98 in Potsdam-Golm

450 in Leipzig

42 % Scientific staff

18 % Administrative staff

17 % Technical assistants / laboratory technicians

10 % Student / scientific assistants

7 % Staff in training

6 % PhD students

44 Mio € project revenue

0,79 Mio € in Rostock

1,88 Mio € in Halle (Saale)

9,21 Mio € in Potsdam-Golm

32,10 Mio € in Leipzig

49 % Industry (21 416 TEUR)

27 % German national and regional government (11 994 TEUR)

21 % Other (9 238 TEUR)

3 % EU (1 334 TEUR)

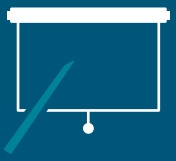
December 31, 2024

Scientific presence and network 2024

146 Industry partners &
165 Research partners

97 Association memberships in various expert associations

105 Publications
5 Book articles
135 Abstracts



67 Teaching activities

43 Graduation publications
8 Doctorates
2 Diploma theses
18 Master theses
15 Bachelor theses

45 Patent families with
229 patents &
89 patent applications
5 Brand families

Detailed information on the key figures and publications can be found on our website at **www.izi.fraunhofer.de/en/publications**

Sponsors and advisory board

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

Sponsors

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

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

Advisory board

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

Members of the advisory board

- Dr. Henrich Guntermann (Chair), European Consortium of Technology Transfer S.A.
- MR'in Dr. Annerose Beck, Saxon State Ministry of Science and the Arts (SMWK), Head of National-Regional Research Centers Administration
- Bettina Berendsen, former Sartorius Stedim Biotech GmbH
- Prof. Dr. Carola Griehl, Anhalt University of Applied Sciences, Köthen, Department of Applied Biosciences and Process Engineering
- Prof. Dr. Hans-Martin Jäck, University Hospital Erlangen, Head of the Molecular Immunology Department
- Prof. Dr. Ulrich Kalinke, TWINCORE - Zentrum für Experimentelle und Klinische Infektionsforschung GmbH
- Dr. Markus Kaymer, Beckman Coulter GmbH
- Prof. Dr. Markus Löffler, Leipzig University, Institute for Medical Informatics, Statistics and Epidemiology
- Dr. Lorenz Mayr, Mayr BioMedTech Consulting, Switzerland
- Dr. Kai Pinkernell, Dr. Falk Pharma GmbH
- Prof. Dr. Uwe Platzbecker, University of Leipzig Medical Center, Department for Hematology, Cell Therapy and Hemostaseology
- Dr. Inge Schlotzhauer, Ministry of Science, Research and Culture of the State of Brandenburg, Potsdam
- Prof. Dr. Nina Worel, University Clinic for Transfusion Medicine and Cell Therapy, Vienna, Austria

The Fraunhofer-Gesellschaft

The Fraunhofer-Gesellschaft, based in Germany, is a leading applied research organization. It plays a crucial role in the innovation process by prioritizing research in key future technologies and transferring its research findings to industry in order to strengthen Germany as an economic hub as well as for the benefit of society.

As an important customer group, small- and medium-sized companies in particular tap into Fraunhofer's expertise and resources to develop new technologies and maintain their competitiveness. For years, Fraunhofer has been one of the most active patent applicants in Germany and Europe. The research organization is therefore developing an extensive, international patent portfolio in various technology sectors, primarily as a basis for transferring technology through research projects, spin-offs and licensing. In this way, Fraunhofer experts support industry partners from ideation to market launch, and Fraunhofer's interdisciplinary and international collaboration in specific market environments addresses social objectives in important technology areas. Fraunhofer also promotes research into key technologies that are vital for society as a whole by applying specific, interdisciplinary and international collaboration geared to the needs of the market. Examples include technologies for the energy transition, cybersecurity and underlying models for generative artificial intelligence. Fraunhofer is an attractive and established party for public-private partnerships and also makes a significant contribution to strengthening Germany as a hub for innovation and ensuring its viability in the future. Its activities create jobs in Germany, boost investment effects in the private sector and increase the social acceptance of new technology. International collaboration projects with excellent research partners and companies across the globe ensure that the Fraunhofer-Gesellschaft remains in direct contact with the most prominent scientific communities and economic areas.

Founded in 1949, the Fraunhofer-Gesellschaft currently operates 76 institutes and research units throughout Germany. Its nearly 32,000 employees, predominantly scientists and engineers, work with an annual business volume of 3.4 billion euros; 3.0 billion euros of this stems from contract research, which is divided into three funding pillars. Fraunhofer generates a share of this from industry and license-fee revenue to a sum of 836 million euros. This high proportion of industrial revenue is Fraunhofer's unique selling point in the German research landscape. The importance of direct collaboration with industry and the private sector that this requires ensures a constant push for innovation in the economy, while at the same time strengthening German and European competitiveness.

Another share of contract research revenue comes from publicly funded research projects. The final share is base funding that is supplied by the German federal and state governments and enables our institutes to develop solutions now that will become relevant to the private sector and society in a few years.

Highly motivated employees are the most important factor in Fraunhofer's success. The research organization therefore creates opportunities for independent, creative and goal-driven work. Fraunhofer fosters professional and personal development in order to provide career opportunities for its employees in the private sector and society at large.

The Fraunhofer-Gesellschaft is a recognized nonprofit named after the Munich scholar Joseph von Fraunhofer (1787–1826), who enjoyed equal success as a scientist, inventor and entrepreneur.

www.fraunhofer.de/en.html

20 YEARS FRAUNHOFER IZI

2005 Foundation of the institute and commissioning of the first laboratories and offices at BioCity Leipzig

2006 Completion of the first clean room facility for the production of cell-based drugs

2007 A staff of more than 100

2008 Commissioning of the main building with 4,131 m² floor space (e.g., laboratories for molecular and cell biology work)

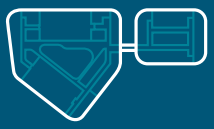
2009 Fraunhofer IZI first certified as a GLP test facility

2011 Establishment of the Department for Extracorporeal Therapy Systems in Rostock

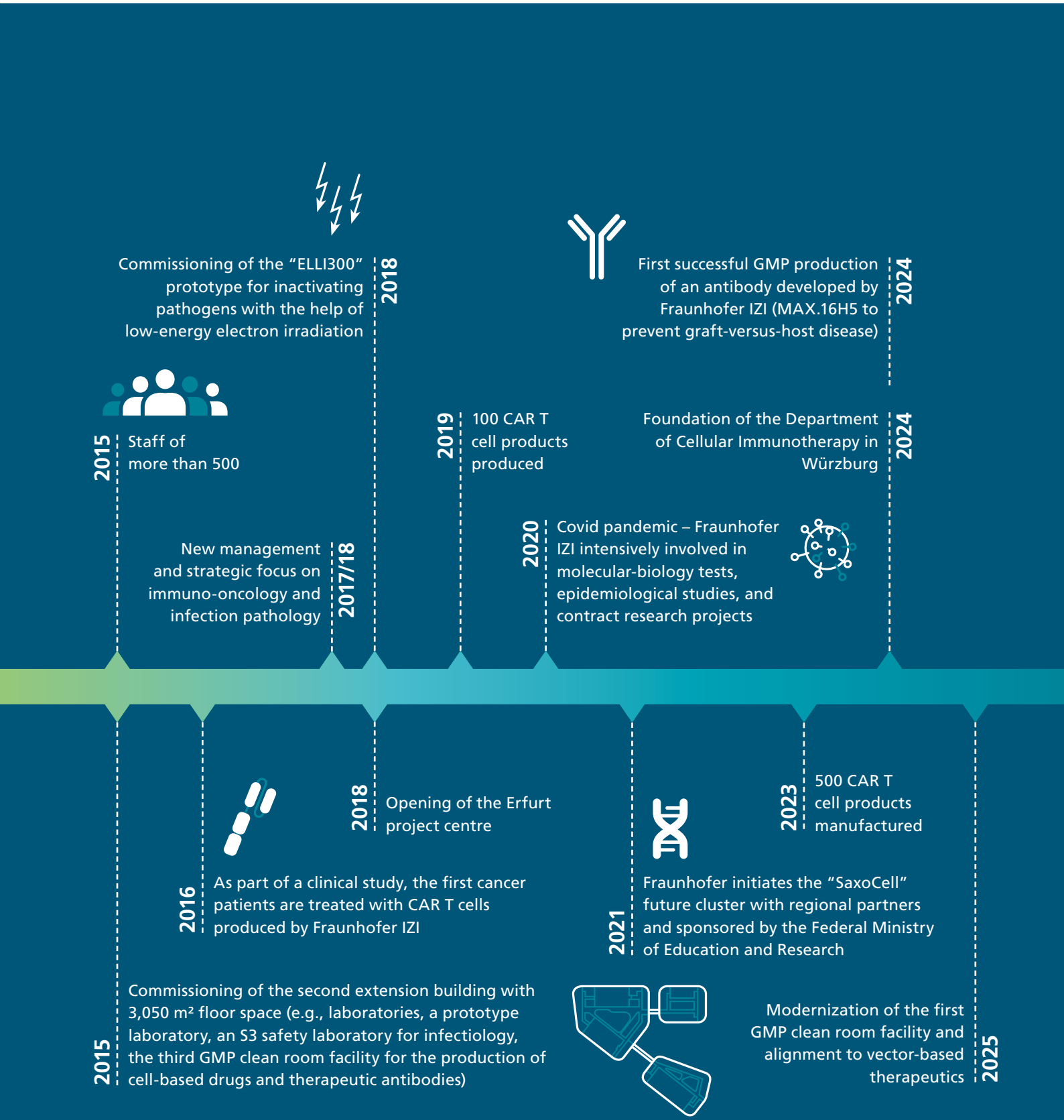
2013 As part of a clinical study, the first cancer patients are treated with cell therapeutics produced by Fraunhofer IZI

2013 Establishment of the Department of Drug Design and Target Validation in Halle (Saale)

2013 Commissioning of the first extension building with 1,568 m² floor space (e.g., laboratories, animal research centre, the second GMP clean room facility for the production of cell-based drugs)



2014 Integration of the Branch of Institute Bioanalytics and Bioprocessing in Potsdam-Golm


2015
Staff of more than 500
2016
As part of a clinical study, the first cancer patients are treated with CAR T cells produced by Fraunhofer IZI
2017/18
New management and strategic focus on immuno-oncology and infection pathology
2018
Commissioning of the "ELLI300" prototype for inactivating pathogens with the help of low-energy electron irradiation
2018
Opening of the Erfurt project centre
2019
100 CAR T cell products produced
2020
Covid pandemic – Fraunhofer IZI intensively involved in molecular-biology tests, epidemiological studies, and contract research projects
2021
Fraunhofer initiates the "SaxoCell" future cluster with regional partners and sponsored by the Federal Ministry of Education and Research
2023
500 CAR T cell products manufactured
2024
First successful GMP production of an antibody developed by Fraunhofer IZI (MAX.16H5 to prevent graft-versus-host disease)
2024
Foundation of the Department of Cellular Immunotherapy in Würzburg
2015
Commissioning of the second extension building with 3,050 m² floor space (e.g., laboratories, a prototype laboratory, an S3 safety laboratory for infectiology, the third GMP clean room facility for the production of cell-based drugs and therapeutic antibodies)
2025
Modernization of the first GMP clean room facility and alignment to vector-based therapeutics

20 YEARS FRAUNHOFER IZI

"Over 20 years, we have developed a modern, as well as complex, research infrastructure. Its maintenance and continuous modernization create new challenges for us every day – but the entire team are passionate about tackling those challenges together."

Dirk Peisker
Member of the technical team and an employee from day 1, joined Fraunhofer IZI in 2005

"It has been, and continues to be, fascinating to see the development of cell and gene therapies over the past 20 years and the importance they now have in treating oncological diseases, as well as to discover their future potential. I am proud to contribute to this development together with our team."

Gerno Schmiedeknecht
Head of the Department of GMP Cell and Gene Therapy, joined Fraunhofer IZI in 2005

"I still remember my first days here at the institute: There were only a few of use and, at lunch time, we all sat around one table – it felt like a new beginning. The vision of the institute started to take shape along with the modern research buildings which were added one after the other."

Ulrike Scholz
Member of the technical staff at the Preclinical Development and Validation Team, joined Fraunhofer IZI in 2006

"Even after 10 years, I still find every new project fascinating. This applies, in particular, to how we, as a team, consider scientific-technological approaches and solve challenges together."

Steffen Jakob
Member of the technical staff at Vaccination Technologies, joined Fraunhofer IZI in 2015

"Our works council and the various interest groups at Fraunhofer IZI are actively working to ensure that the atmosphere of cooperation and a motivating work environment are supported and sustainably strengthened even during challenging times and in difficult situations."

Wenke Fröhlich
Member of the technical staff at Diagnostics and chair of the works council, joined Fraunhofer IZI in 2008

"The development of our institute is always tied to that of its staff. I enjoy actively supporting our colleagues' professional and personal development at the institute."

Janine Schulz-Orawetz
Staff Development, joined Fraunhofer IZI in 2021

"Regardless of whether you work in IT, at the laboratory or in administration – here, everyone helps to bring innovations to life. I congratulate the institute and, along with it, all the colleagues who have helped shape the institute and made it successful over the past twenty years."

Anja Bochmann-Seidel
Head of Administration, joined Fraunhofer IZI in 2008

"Setting up a new Fraunhofer Institute covering a young research area and operating in a field with difficult framework conditions for clinical translation in 2005 certainly took a lot of energy and conviction. For this reason, I am extremely proud to see the fruits of this labor – 600 highly motivated employees and countless innovative ideas. Allow me to congratulate – as well as thank – all those who have contributed to this and, of course, I hope that this success will continue for, at least, the next twenty years."

Professor Emeritus Dr. Frank Emmrich
Initiator and founding director of Fraunhofer IZI

"When I had the honor of taking over the management of this superb institute in late 2017, I faced the challenge of leading this institute in its scientific and commercial heyday into a successful future. In this effort, I have the support of an excellent scientific and caring political environment, as well as an exceptional team day after day. I would like to express my heartfelt thanks for this support."

Prof. Dr. Dr. Ulrike Köhl
Director, joined Fraunhofer IZI in 2017

Locations and departments

Headquarter in Leipzig

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 Vaccines, 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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Department of GMP Cell and Gene Therapy (Leipzig site)

The Department of GMP Cell and Gene Therapy operates Fraunhofer IZI's two modern GMP facilities consisting of six separate clean room suites (altogether 13 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 105 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

- Manufacturing and quality control of ATMPs
- Update of the assortment list of the general manufacturing authorization according to § 13 AMG
- GMP process and method transfer
- Quality assurance in accordance with Good Manufacturing Practice (GMP)
- Operation of 632 m² clean rooms
- Support in preparing the Investigator Medicinal Product Dossier (IMPD)

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Cell and Gene Therapy Development and Clinical Gene Transfer (Leipzig site)

The Department of Cell and Gene Therapy Development and Clinical Gene Transfer researches and develops cell and gene therapy technologies and realizes the transfer of manufacturing processes from an experimental stage to GMP-compliant procedures.

The focus is on antigen-specific T cells, CAR-T cells, CAR-NK cells, dendritic cells, mesenchymal stromal cells and tissue engineering products.

The department's competencies, which build on each other, include research and development, preclinical evaluation and GMP process development for cell and gene therapies up to transfer into pharmaceutical manufacturing processes. Manufacturing parameters and quality controls can be tested and optimized flexibly and cost-efficiently.

New technologies (including digitalization, artificial intelligence, automation) as well as clinically relevant application aspects are considered at all stages of development.

In addition, biomolecules such as antibodies, proteins, enzymes and, in the future, viral vectors are produced in pharmaceutical quality in a separate GMP manufacturing unit.

After successful process optimization, investigational medicinal products can be produced by the Department of GMP Cell and Gene Therapy and further accompanied until approval.

Core competencies

- GMP process development and transfer for cell and gene therapy manufacturing
- mRNA technology
- Specialist expertise in internal medicine / hematology / oncology / immunology
- Process optimization and automation
- Good Manufacturing Practice (GMP) evaluation for cell and gene therapy manufacturing
- Quality assurance
- GMP-compliant equipment and processes
- Clinical trial planning
- CAR-T/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)
- Non-viral gene transfer
- Transposon / transposase technologies
- Gene editing

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www.izi.fraunhofer.de/en/departments/leipzig-location/cell-and-gene-therapy-development

Preclinical Development and Validation (Leipzig site)

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 Fraunhofer 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, preclinical studies (even those in other Fraunhofer IZI departments) can be performed under GLP.

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, Luminex®, lateral flow assays, flow cytometry).
- Identifying and validating new protein biomarkers for diagnosis and therapy (in particular using LC-MS-based proteomics) of chronic-inflammatory and tumor diseases, as well as for the sector of regenerative medicine.
- Developing human monoclonal antibodies to be directed against new therapeutic tumor targets (triple-negative breast cancer).

Core competencies

- Preclinical studies
- Good laboratory practice (GLP)
- Immunotoxicology (study design and implementation)
- Efficacy and safety studies for ATMPs and class-3 medical devices
- Protein biomarker (identification and validation)
- Antibody development (therapy)
- Antibody and immunoassay development (diagnostics)
- Histopathology, toxicopathology
- Chronic inflammatory bowel disease (therapy development)
- Triple-negative breast cancer (therapy development)
- LC-MS based proteomics

Contact

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www.izi.fraunhofer.de/en/departments/leipzig-location/preclinical-development-and-validation

Infection Research and Diagnostics (Leipzig site)

The Department of Infection Research and Diagnostics researches and develops technologies for the prevention, treatment and diagnosis of infectious diseases.

Innovative technology platforms are available for the development of vaccines, e.g. novel inactivation procedures or nucleic acid-based methods. An S3 laboratory enables work with highly infectious pathogens. Diagnostic and analytical procedures are developed on the basis of molecular and immunodiagnostic tests. Particular expertise exists in the design and manufacture of point-of-care systems that enable simple and robust analysis outside of clinical laboratories. Comprehensive competencies in the development of in vivo and in vitro model systems as well as modern imaging techniques complement the department's range of services in the development of modern active substances and diagnostics.

Core competencies

- Vaccine development
- Infection models
- Inactivation of pathogens
- Working with highly infectious pathogens
- Drug testing
- Antimicrobial therapies
- Serological test systems
- Identification and characterization of bacteriophages
- Lab-on-Chip
- Organ-on-Chip
- Experimental imaging

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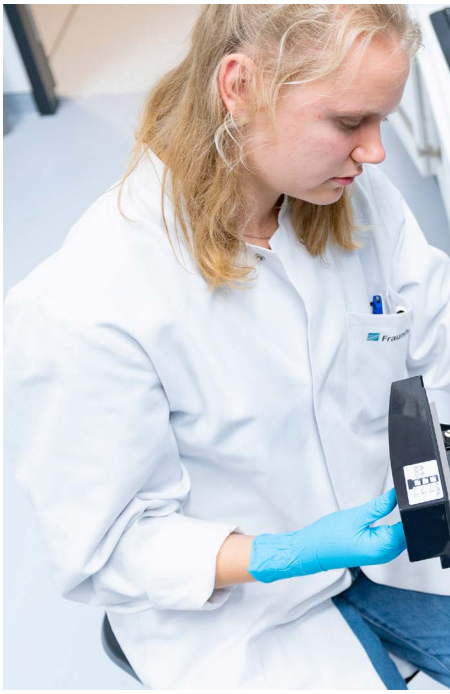
Medical Bioinformatics (Leipzig site)

The Department of Medical Bioinformatics studies and develops computer-based and data-supported technologies for the next generation of precision medicine.

To this end, it combines bio-informatics methods with multimodal individual-cell analysis. This permits the characterization of a large number of molecular and cellular markers in individual cells as well as their biomechanical properties. The department develops digital patient twins, biomarkers and biosensors for personalized medicine and formulates new therapeutic target molecules with the help of machine learning and computer-supported biomedicine.



Selected processes used by the department are implemented in line with a certified quality management system (ISO 9001:2015). Software components are implemented according to IEC 62304 and ISO 14971 to ensure that the computer-based methods developed can be used in the healthcare sector.

The department also supports preclinical development and assessment of novel therapies by providing detailed insights into their modes of action and assists customers and partners in planning and executing clinical studies through tailor-made bioinformatics workflows, multi-modal individual-cell analyses, and biomechanical cell characteristics.

Core competencies

- Transcriptome and immunome analyses
- Next-generation-diagnostics
- Bioinformatics
- Biomarker identification
- Quality assurance according to DIN EN ISO 9001:2015

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Extracorporeal Therapy Systems (Rostock site)

The Department of Extracorporeal Therapy Systems focuses on the development and evaluation of extracorporeal (outside the body), organ-supporting 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

Contact

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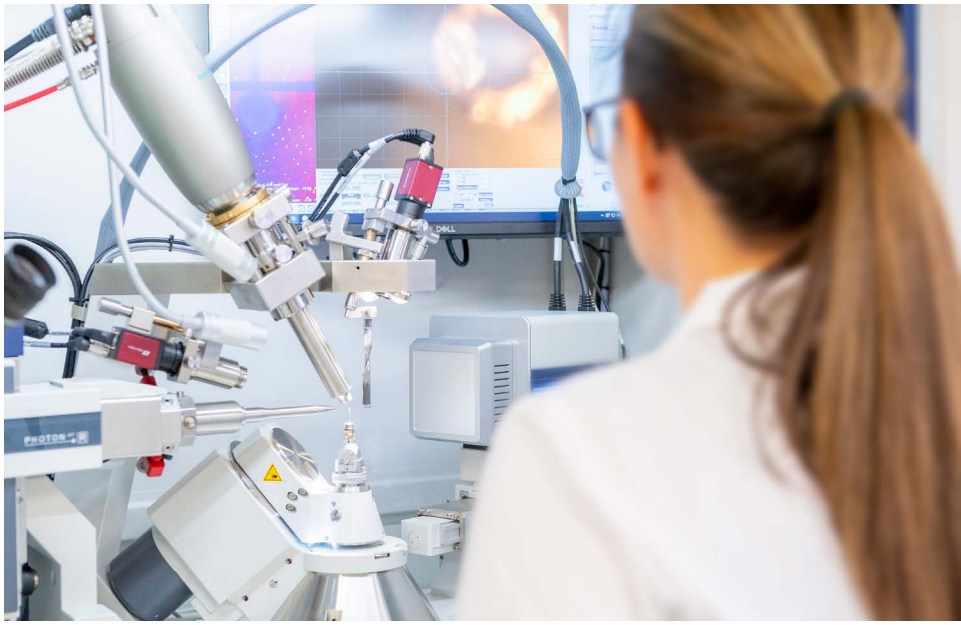
www.izi.fraunhofer.de/en/departments/rostock-location/extracorporeal-therapy-systems

Drug Design and Target Validation (Halle (Saale) site)

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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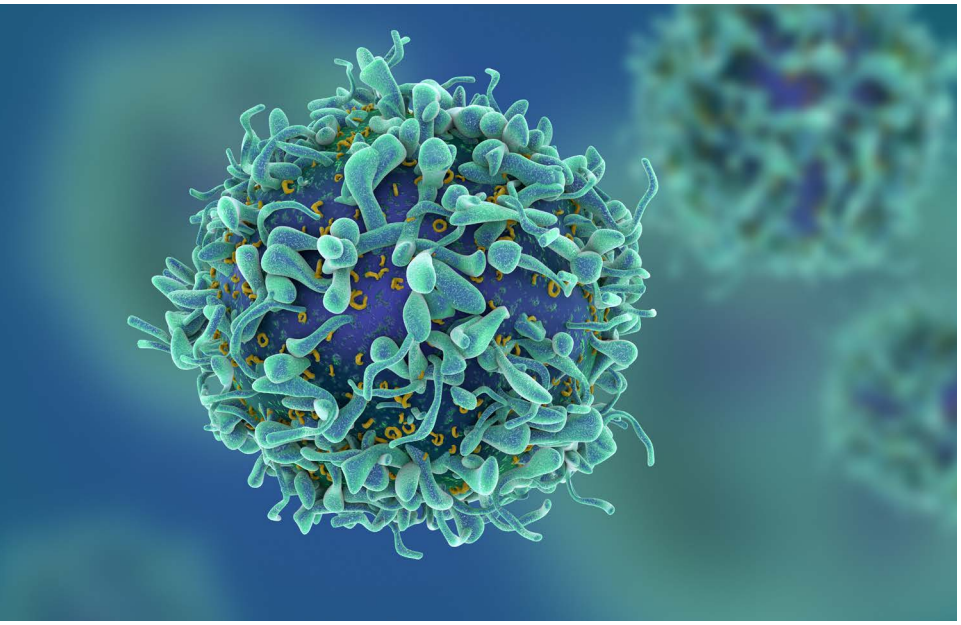
www.izi.fraunhofer.de/en/departments/halle-location/department-of-drug-design-and-target-validation



Cellular Immunotherapy (Würzburg site)

The Department of Cellular Immunotherapy researches and develops new forms of therapy for the treatment of various cancers. The focus here is on the combination of different, genetically modified immune cells within a drug with the aim of improving effectiveness and long-term efficacy. In addition, new therapeutically relevant target structures on cancer cells are identified and transferred to the application of cell-based immunotherapies. Innovative manufacturing technologies based on non-viral gene transfer are being developed and validated with the aim of reducing the costs and time required for the production of cell and gene therapeutics and increasing their general availability.

The team has extensive expertise in the preclinical and clinical analysis of genetically modified immune cells. Through close collaboration with the University Hospital of Würzburg, the team has access to an extensive clinical trial network to bring innovative therapies to the clinic quickly and efficiently. With a broad portfolio of analytical and diagnostic methods, the team supports the production and development of CAR-modified immune cells, from research and development to final product analysis.

Core competencies

- Development and testing of new CAR designs
- Assessment of the effectiveness and specificity of new CAR designs
- Evaluation of new reagents to activate and cultivate immune cells
- Development and implementation of alternative cell culture systems
- Testing and validation of devices for the development and production of cellular immune therapies

Contact

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Branch Bioanalytics and Bioprocesses (Potsdam-Golm site)

The Bioanalytics and Bioprocesses Branch in Potsdam-Golm works on technological solutions for biomedicine and diagnostics as well as for biotechnology and bioproduction.

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

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

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

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Fraunhofer Center Erfurt (formerly Fraunhofer MEOS) (Erfurt site)

The Fraunhofer Center in Erfurt comprises the interdisciplinary work of the three Fraunhofer Institutes for Photonic Microsystems IPMS, for Applied Optics and Precision Engineering IOF and for Cell Therapy and Immunology IZI. It conducts customer- and application specific research and development primarily for the markets of medical technology, analytics, diagnostics, biotechnology, biophotonics, pharmaceuticals, health and aging, as well as the food industry.

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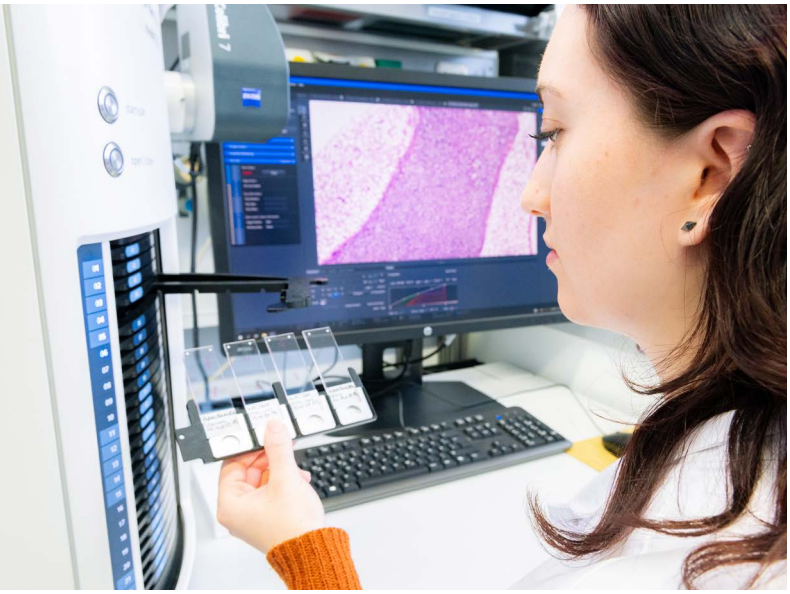
Central facilities

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 for testing category 9 since 2009. Among other things, this includes safety tests for ATMP immunotoxicity / immunogenicity, biodistribution and tumorigenicity in vitro and in vivo. Testing category 2 was added to the portfolio in 2023, which includes tests to determine toxicological properties.

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.



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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 performs the manufacture of investigational medicinal products for clinical trials.

Advanced Therapy Medicinal Products (ATMPs)
The Fraunhofer IZI maintains two GMP-compliant clean room facilities for the manufacturing of 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. 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 room (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 the update of the assortment list of the general official manufacturing authorization pursuant to section 13 of the German Drug Act (AMG).

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Why are GMP and GLP important?

A clinical trial of a new drug candidate is an essential step on the way to approval. Since the 12th revision of the "Arzneimittel-gesetz 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 trial. 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.

Advanced Analytics Technology Platform

The Advanced Analytics technology platform bundles existing analytical competencies and technologies for data evaluation and interpretation at Fraunhofer IZI.

With a broad portfolio of state-of-the-art technologies and corresponding expertise, customers and partners are supported with comprehensive analyses in the development of a wide range of therapeutics and diagnostics.

Assays can be developed at different scales or complete proof-of-concept studies can be realized according to customer-specific requirements. The platform's subdivisions work together in an integrative manner, from study design and experiment execution to multi-modal data evaluation.

The Advanced Analytics technology platform bundles the following competencies:

Chromatography and mass spectrometry

- Preparative chromatographic separations (RP, SEC, IC) Identity determination of isolated proteins by peptide mass fingerprinting (PMF) and MS/MS analyses
- MS-based elucidation and detection of protein modifications and protein interactions
- Consulting, sample preparation, performance and evaluation of proteomics studies
- Determination of toxins and metabolites in biofluids by Multiple Reaction Monitoring (MRM)
- Analysis of active substances and their degradation products by MRM
- Characterization of ssDNA and ssDNA conjugates

Flow cytometry and FACS

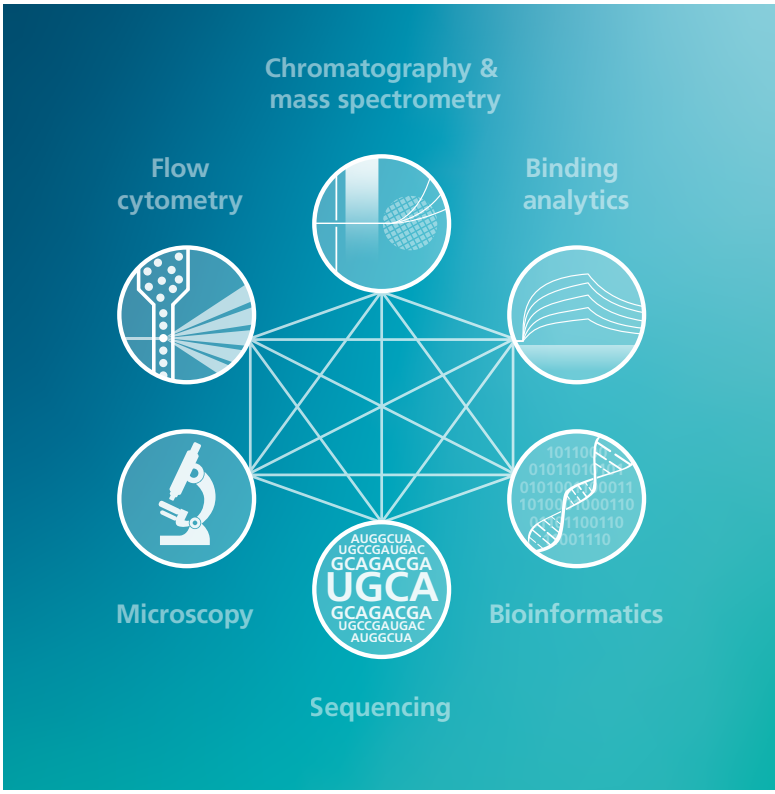
- Cell-based assays (immunophenotyping, apoptosis, internalization, proliferation / cell cycle, migration, degranulation)
- Bacteria-binding assay
- Cell sorting

Microscopy / imaging

- Multimodal imaging for preclinical research
- Brightfield, live cell, fluorescence and confocal laser scanning microscopy
- Slide scanning services
- In vivo imaging via magnetic resonance imaging (MRI), computed tomography (CT) and optical imaging (BLI / FLI) for small animals
- Evaluation of various (also correlative) image data
- Microscopy training of users and technical support

Sequencing

- Classical next generation sequenzing (NGS) methods
  - Whole transcriptome sequencing (mRNA and total RNA)
  - Whole genome and exome sequencing
  - Small genome and 16S sequencing
- Advanced NGS methods
  - Single-cell multi-omics
  - Spatial transcriptomics



Bioinformatics and machine learning

- Machine learning & multi-omics: Machine learning & AI for deep molecular data; multi-modal data science; statistical learning; integrative bioinformatics; pipeline development
- Software components for IVDs: Development of algorithms and software components for medical devices in particular in vitro diagnostic devices (IVDs) and lab developed tests

Contact
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Center for Experimental Medicine

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

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

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

All experimental work can be carried out under practically sterile conditions. 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

- 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

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. The ventilation system guarantees eight air changes per hour with an air flow volume of up to 1500 m³/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, a climate cabinet 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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Research area immuno-oncology

Selected projects

The research area immuno-oncology

For a few years now, immuno-oncology has been complementing the classic methods of cancer therapy, radiotherapy, chemotherapy and surgery. Here, medicine makes use of the natural function of the immune system to eliminate foreign and degenerate cells via a wide variety of mechanisms. With the research area immuno-oncology, Fraunhofer IZI supports partners in the development and translation of innovative immunotherapies.

R&D focus

- ATMP development
- Preclinical development of cell and gene therapies (efficacy and safety analysis)
- Cell analysis, assay development and diagnostics
- GMP process development / process transfer
- Manufacturing of investigational medicinal products

In-a-box screening system for CAR-T cell therapy – "CAR Finder" technology

Chimeric antigen receptor (CAR) cell therapeutics are considered to be a groundbreaking innovation in cancer treatment. So far, they have only been approved for a few hematological types of cancer. However, numerous preclinical studies, as well as a growing number of clinical studies,

have confirmed the technology's enormous potential for other oncological indications, and beyond.

Today, approved CAR cell therapeutics are manufactured by means of a stable genetic modification of immune cells via viral transduction. But the viral generation of CAR immune cells is a very time-, material- and cost-intensive procedure and, for this reason, it is not suitable for extensive testing of new CAR designs using screening methods.

To remedy this, Fraunhofer IZI has developed a time- and cost-saving method based on mRNA transfection for the efficient generation of new CAR immune cells. This method permits high throughput screening for the fast identification of optimal candidates for new CAR cell therapeutics and functional testing for anti-tumor effectiveness. This will significantly speed up preclinical development.

The new method has now been patented and is available for partners from both academic and industrial research and can be easily and cost-effectively adapted to other tumor types or diseases, such as autoimmune diseases or fibroses.

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CAR Factory – A high-performance platform for the development of genetically optimized CAR-T and CAR-NK cell therapies for treating cancer

This project aims to provide a technology platform to accelerate the preclinical development of CAR-modified immune cell therapies. The efforts will focus on types of cancer which are difficult to treat and on solid tumors.

The targeted combination of CAR modifications and gene editing aims to improve anti-tumor activity, tumor infiltration and longevity of T and NK cells and to overcome immunosuppressive factors in the tumor environment.

Deutsche Krebshilfe
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To achieve this, the consortium will use a broad range of identified target molecules to generate CAR immune cell products, which will be developed and validated as part of this project.

Fraunhofer IZI is contributing its expertise in the development of CAR-modified T and NK cell therapies and in non-viral gene transfer technologies (Sleeping Beauty transposon). Another field of action comprises the development of pharmaceutical manufacturing processes for immune therapies as the basis for clinical testing.

Partners
Frankfurt University Hospital (Coordination); University Hospital of Würzburg (Coordination); Freiburg University Hospital

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Establishment of a GMP-compliant cell line for the production of viral vectors

This project aims to produce a stable human cell line for the efficient, cost-effective and safe production of clinical test specimens of adeno-associated viral vectors (AAV). To this end, as a first step, a master cell bank will be established on the basis of HEK293 cells, which will be stably transfected with the help of lentiviral vectors. As a next step, a stable expression system for the AAV vector production is to be developed. In the framework of this project, the genetic information for serotype AAV2 and a vector design which carries an eGFP (enhanced green fluorescent protein) are to be introduced into the HEK293 cells, by way of example.

The cell line will fulfil the regulatory requirements of the Good Manufacturing Practice (GMP) under the EU-GMP Guideline and, therefore, it will be of sufficiently high quality for use as a source material for drugs.

As a result, a reliable and efficiently scalable system will be established in line with the pharmaceutical industry's high quality requirements and will optimize the production of AAV vectors for use in gene therapy.

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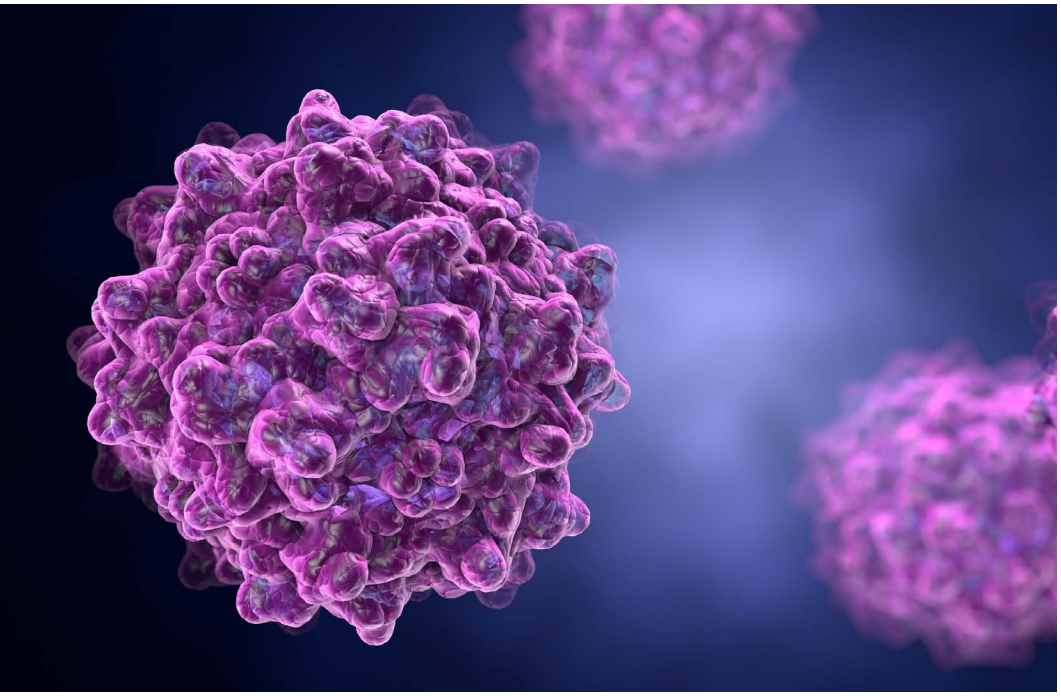

Gefördert aus Mitteln der Europäischen Union

Europa fördert Sachsen.
EFRE
Europäischer Fonds für regionale Entwicklung

This project is co-financed by tax revenues on the basis of the budget approved by members of the Saxon state parliament.

Preclinical and clinical development of a novel CAR-T cell therapy for the treatment of multiple myeloma and clear cell renal cell carcinoma

CAR-T cell therapy is based on the principle of equipping immune cells (T cells) with an artificial chimeric antigen receptor (CAR) by genetic modification. This enables the immune cells to identify specific surface structures (antigens) on cancer or other target cells and to activate a corresponding immune response.

With the ROR2-CAR-T cell therapy, scientists at the University Hospital of Würzburg have developed an immunotherapy that differs from previously approved therapies both in the type of genetic modification and the target antigen addressed.

The ROR2 protein is a transmembrane receptor that plays an important role especially during embryonic development. It is normally not expressed, or only very slightly expressed, in adult, healthy cells. However, in some cancers, including multiple myeloma and clear cell renal cell carcinoma, it is highly expressed on the cancer cells in question. This makes the antigen a suitable target for appropriately targeted CAR-T cells.

In this project, a new method for the production of autologous CAR-T cells, which is still being tested, is used. The genetic modification of the patient's own T cells is carried out via a non-viral gene transfer, which, compared to viral gene transfer, will enable a simpler, more scalable and thus less expensive production process.

Fraunhofer IZI is responsible for two main areas within the project. On the one hand, the pre-clinical examination of the safety and effectiveness of the novel CAR-T cell product, including establishing the expression of the ROR2 target molecule in healthy tissues and identifying potentially cross-reacting epitopes (GLP study). On the other hand, the pharmaceutical manufacturing of the investigational medicinal products for the clinical trial, including the prior establishment and validation of the manufacturing process as well as the safety-relevant quality controls.

The project is funded by the Federal Ministry of Education and Research.

Partners
University Hospital of Würzburg; T-CURX GmbH

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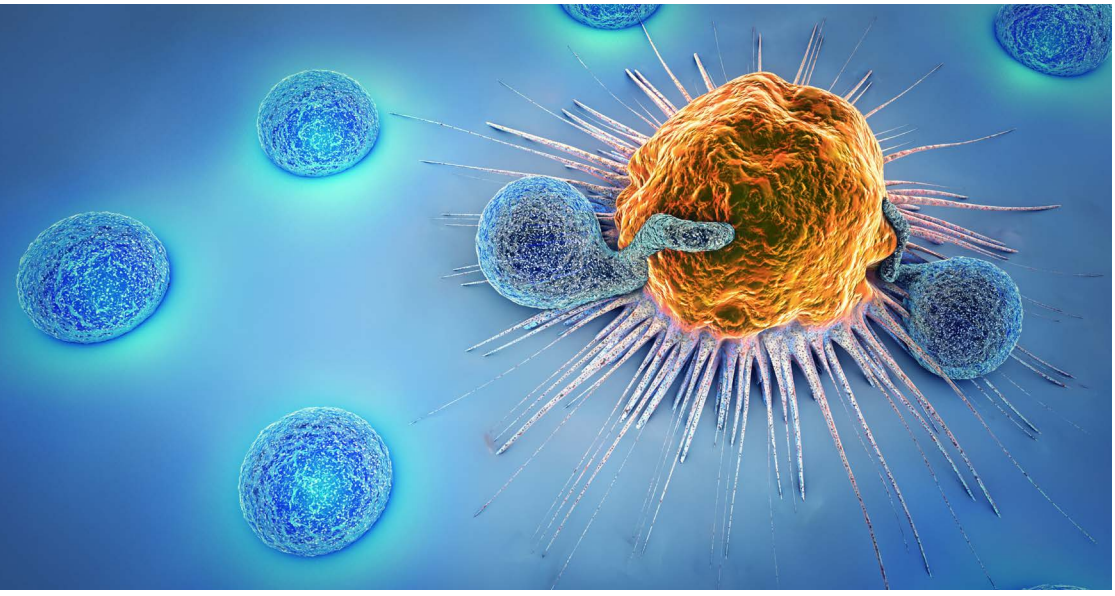

SPONSORED BY THE
Federal Ministry of Education and Research

Inactivation of therapeutic immune cells by low-energy electron irradiation

This project aims to develop innovative irradiation processes for the production of modern cell and gene therapeutics.

Low-energy electron irradiation (LEEI) is an irradiation method suitable for the efficient inactivation of pathogens (such as viruses and bacteria) and eukaryotic cells. This inactivation method is based on the destruction of the genetic information (nucleic acids).

The new method has been patented, and Fraunhofer IZI has a research prototype which is unique worldwide, and which can be used to develop this irradiation technology and adapt it to various applications.

The project will evaluate low-energy electron irradiation for two specific application scenarios: The first application scenario will include the irradiation of leukocytes as an alternative method in extracorporeal photophoresis. Under the current method, the cells are treated using ultraviolet radiation with the addition of a photosensitiser (a light-activated substance). This treatment is, e.g., used in graft-versus-host disease, the main complication after allogenic hematopoietic cell transplants. If low-energy electron irradiation is used, the addition of a photosensitizer (which involves side effects) is not necessary.

The second application addresses the production of NK cell-based immune therapeutics. Unlike cell therapeutics from T effector cells (such as CAR-T cells), natural killer cells have to be co-cultivated in a complex process using feeder cells to achieve the clinically required quantities of therapeutic cells. If feeder cells are used in GMP production processes, their growth is usually inhibited using irradiation methods for safety reasons. The suitability of LEEI as an alternative inactivation method for feeder cells will be examined as part of this project.

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Gefördert aus Mitteln der Europäischen Union

Europa fördert Sachsen.
EFRE
Europäischer Fonds für regionale Entwicklung

This project is co-financed by tax revenues on the basis of the budget approved by members of the Saxon state parliament.

Fraunhofer ATTRACT program “CAR-Duett“

Although CAR-T cell therapy achieves very good response rates for certain types of leukemia and lymphoma, in part with lasting remission, some patients suffer recurrences. These are usually due to mutated leukemia cells which have lost the therapeutically relevant tumor antigen. A combination of various CAR-modified immune cells are designed to expand the spectrum of efficiency and overcome mechanisms that lead to tumor resistance. Under this project, CAR-T as part of the adaptive immune system cells are formulated in the form of a duet (DUETT) with CAR-NK cells as part of the innate immune system.

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MinAAVAb – AAV-mediated expression of therapeutic antibodies via minimally invasive application

Antibody treatments have been established to treat various diseases, such as autoimmune disorders, tumors, and infections. However, long-term and lastingly effective treatment based on the systemic administration of functional antibodies involves high costs for healthcare systems.

Adeno-associated viral vectors (AAV) constitute a potential alternative. They can be used to introduce therapeutic genes into target cells. They do not cause any illness; they infect specific cell types and are not incorporated into the human genome. These characteristics make them a safe and effective vector for genetic therapy. After successful transduction (integration into the target cells), AAV containing the blueprint for therapeutic antibodies can be permanently produced by the human body.

The project aims to develop and evaluate novel, minimally invasive forms of application for AAV-based medications. As part of the proof-of-concept study, the AAV will be optimized and used to express therapeutic antibodies.

Partners
Fraunhofer ITEM; Fraunhofer ITMP; Hanover Medical School (MHH)

Support
This project is financed as part of the Fraunhofer Cluster of Excellence for Immune-Mediated Diseases (CIMD).

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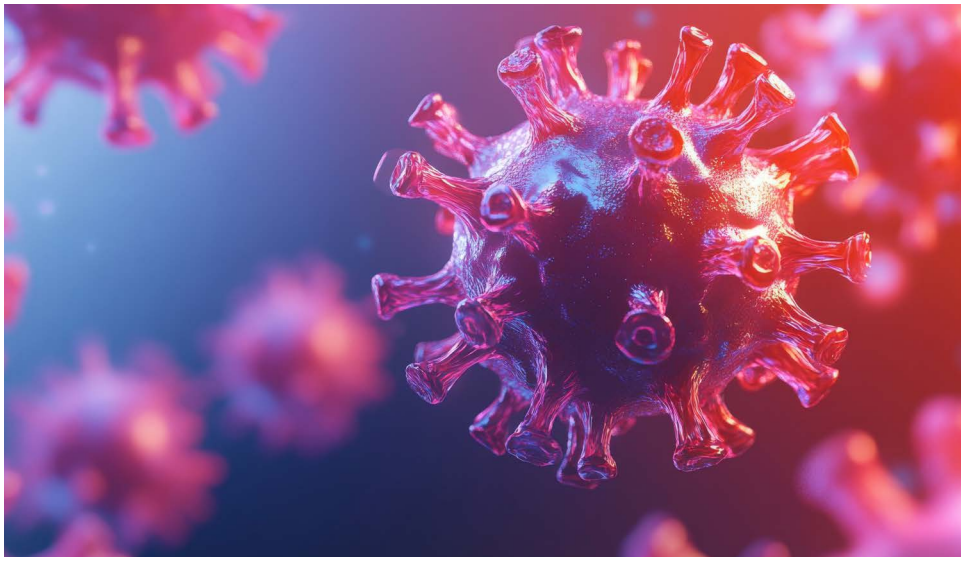

Next generation transposon tools

The current protocols for the autologous ex-vivo gene and cell therapy comprise a work-, time- and cost-intensive supply chain. The patients' cells are usually extracted in a specialized clinical center and delivered to a central production facility, where the cells are genetically modified, expanded and subjected to quality controls. After this, the cryopreserved cell product is returned to the hospital, where the treatment is carried out. At present, production protocols are being developed to significantly reduce production times and costs in order to cover the growing future demand and facilitate comprehensive access to cell and gene therapies.

The current methods for genetic engineering of therapeutic cell products have a number of limitations. These include the lack of long-term expression of transgenes, the risk of insertional oncogenesis and other harmful mutations of the recipient cells' genome. Moreover, the production of genetic vectors of pharmaceutical quality involves considerable costs.

Non-viral gene transfer technologies constitute a promising option to make the production of genetically modified cells considerably more cost effective.

The simplest gene transfer vehicles known from nature are transposons. Genome integration using transposase enzymes turns transposons into unique non-viral vector systems, which can be used as tools for various applications in genetic engineering, including gene therapy. One of the best characterized transposons, the Sleeping Beauty transposon, offers great potential for the development of safe and commercially viable cell therapeutics. So far, however, the sub-optimal efficiency of genome integration in certain human cell types, the insufficiently controlled transposase expression in cells and the risk of

insertional mutagenesis as a result of random genome-wide integration still constitute relevant limitations of the technology.

This project aims to improve the effectiveness and safety of the Sleeping Beauty transposon technology and prepare it for clinical development.

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AIDPATH – AI powered, Decentralized Production for Advanced Therapies in the Hospital

So far, the provision of modern cell and gene therapies, such as the CAR-T cell therapy, requires staff- and time-intensive production processes in centralized and specialized production facilities.

This results in a number of challenges regarding availability, efficiency and logistics which have to be optimized to make this treatment available on a broader basis.

An international consortium subsidized by the EU addresses essential parts of these challenges through its AIDPATH (AI powered, Decentralized Production for Advanced Therapies in the Hospital) project. This project aims to develop a largely automated production platform for CAR-T cells, which can be integrated within a (decentralized) hospital environment. The integration of artificial intelligence is designed to enable the platform to produce CAR-T cells close to the patients and without specialized staff and, as a result, to reduce both production time and costs. Fraunhofer IZI is contributing its expertise in the GMP-compliant production and regulation of cell-based therapeutics. During the reporting year, the first prototype was installed at the University Hospital of Würzburg where it is being tested and optimized by staff at the Fraunhofer IZI Department of Cellular Immunotherapy.

Partners
AglarisCell SL, Tres Cantos; Foundation for Research and Technology - Hellas, (FORTH), Patras; Fraunhofer Institute for Production Technology IPT, Aachen; Fraunhofer Institute for Cell Therapy and Immunology IZI, Leipzig; Fundacio Clinic per a la recerca Biomedica, Barcelona; IRIS Technology Solutions, Sociedad Limitada, Madrid; Ortec Optimization Technology B.V., Zoetermeer; Panaxea BV, Amsterdam; Red Alert Labs, Maisons-Alfort; Sartorius CellGenix GmbH, Freiburg; SZTAKI Institute for Computer Science and Control, Budapest; University Hospital of Würzburg, Würzburg; University College London, London

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www.sciencrew.com/c/6499?title=AIDPATH

Horizon 2020
European Union Funding
for Research & Innovation

SaxoCell SB-Tract

The Sleeping Beauty transposon system is a powerful tool permitting stable genetic engineering of T cells without involving viral vectors. This aims to ensure improved safety profiles as well as more cost- and time-efficient production processes for T cell-based therapeutics.

As part of the SB-TRACT project, preconditions for the clinical development of CAR-T and TCR-T cell therapies are being developed. This includes the optimization of the Sleeping Beauty technology and the development of preclinical lead candidates of transposon-modified T cells for the treatment of solid tumors. In addition to the development of suitable production protocols for the (partly) automatic production on commercially available production platforms, technical and regulatory obstacles are to be identified and solution strategies for later development phases are to be developed.

As part of this project, Fraunhofer IZI is contributing its expertise in the field of non-viral gene transfer methods and the development of GMP-compliant production processes for cell and gene therapeutics.

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SaxoCell SafeTy

In some instances, T cell-based treatments for hematological cancers involve serious side effects. While the graft-versus-host disease (GvHD) constitutes the main complication in allogenic cell therapies, such as hematopoietic stem cell transplants, the cytokine release syndrome constitutes a dangerous overreaction of the immune system following autologous CAR-T cell treatment.

The SafeTy project examines novel technologies for their suitability for treatment and the prevention of this side effect.

This includes clinical testing of ATMPs Palintra® for the prevention of GvHD and studies as to whether this can also be transferred to allogenic CAR-T cell therapies. Another aim is to examine whether the technology of low-energy electron irradiation is suitable for GvHD treatment.

Moreover, extracorporeal photopheresis technology is being examined as a potential treatment for preventing cytokine release syndrome following autologous CAR-T cell treatment.

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SaxoCell Edit-Save

This project aims to further develop pioneering genome editing methods for cell and gene therapies. These permit the removal, insertion, or modification of DNA sequences in cells. The project will examine various technologies which can be used to engineer the genetic material in (immune) cells to render them useful for therapeutic purposes, e.g., in blood and autoimmune disorders and cancers.

As part of this, Fraunhofer IZI is contributing its expertise in the field of clinical gene transfer. The focus is on non-viral systems, such as lipid nanoparticle transfection using the Sleeping Beauty transposon technology, which is to be used to genetically modify macrophages to develop treatments against autoimmune disorders, e.g., systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) in the future.

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SaxoCell NK-Alliance

Natural killer cells (NK cells) constitute a promising resource for the development of cell-based immune therapies, e.g., to treat cancer and autoimmune disorders. Because of their immunological properties, NK cells are also a candidate for allogenic (i.e. non-patient-specific) treatments, which would provide considerable advantages in terms of production, efficiency, and availability, in addition to their therapeutic potential. In spite of the high potential, a variety of challenges have to be overcome until clinical translation. This, e.g., includes genetic engineering methods to increase efficiency and develop suitable production processes ensuring sufficiently high and clinically relevant cell counts.

The NK Alliance project addresses these aspects and creates the preconditions for the clinical application of NK cell-based therapeutics.

As part of this, Fraunhofer IZI is contributing its expertise in the development of genetically engineered NK cells and GMP-compliant production processes. For example, a GMP-compliant pharmaceutical production process will be established using a CAR-NK cell-based treatment for acute myeloid leukemia and examined for automation options. In addition, various treatment candidates are to be examined for their efficiency and safety in a suitable model system. Likewise, AI technologies will be used to optimize various aspects, such as donor selection, production efficiency, and functionality.

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Research area infectious disease pathology

Selected projects

The research area infectious disease pathology

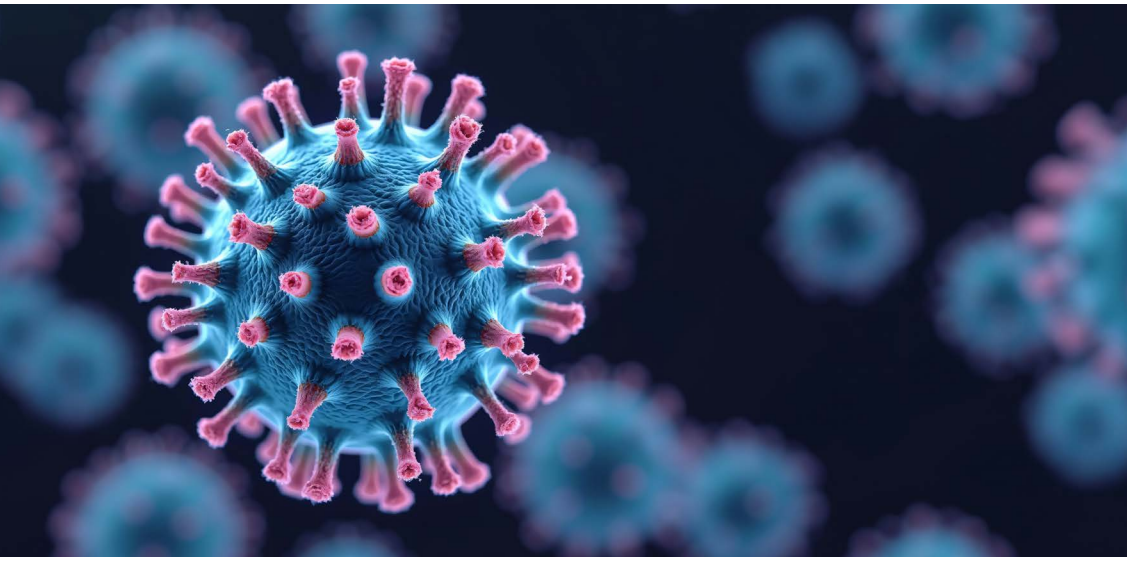
Infectious diseases continue to pose a global threat to human and animal health. Understanding the spread, pathogenesis and possibilities of diagnosis, is essential for their effective control. With the research area infectious disease pathology, Fraunhofer IZI supports partners in the development and translation of technologies for research, diagnostics, prevention and therapy of infectious diseases.

R&D focus

- Preclinical development of active agents and vaccines (efficacy and safety analysis)
- Vaccine technologies
- Drug and material testing
- Assays and diagnostics

Development of a vaccine candidate against the West Nile virus

The West Nile virus (WNV) is a zoonotic flavivirus spread by mosquitoes. The virus primarily circulates among birds, but can also be transmitted to mammals, like humans. Even though, in most cases, an infection only involves mild, cold-like symptoms, it can also cause severe neurological problems, in particular, in older or immunocompromised patients. So far, a human vaccine against the West Nile virus is not available.



The envelope protein (E) is the most important target of neutralizing antibodies and, for this reason, it is of fundamental importance for vaccine development. It is located on the surface of the virus and has a central role at various points of the viral life cycle, especially, when the virus enters the host cells.

The close genetic relationship between WNV and other flaviviruses (such as the Zika virus or the Dengue virus) means that the E proteins are very similar in their sequence and structure. This forms a particular challenge in the development of suitable vaccine candidates. In the case of an infection with other flaviviruses, the antibodies formed as a result of the immunization can lead to cross-reactions, which might amplify the infection and are associated with more severe courses of the disease. This is particularly difficult in regions in which several flaviviruses coexist.

Therefore, the aim is to develop improved protein- and mRNA-based vaccine candidates while avoiding cross-reactions with similar viruses.

Most cross-reactive antibodies bind the E protein in an area which is almost identical in most other flaviviruses, the so-called fusion loop. Therefore, a possible solution for immunization comprises the use of antigens in which this area has either been mutated or eliminated altogether. It was proven in an animal model that corresponding antigens induce a largely protective immune response. An analysis of the neutralizing antibodies showed a significantly reduced cross-reactivity with other flaviviruses, compared to the wild-type protein.

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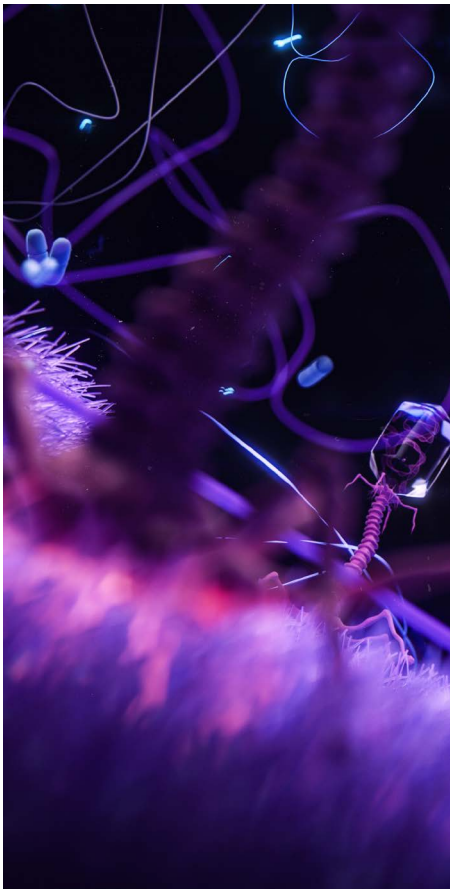
COX-SAVE – Development of a safe Q fever vaccine for ruminants using electron-beam-inactivated Coxiella

Coxiellosis, also known as Q fever, is a global problem in breeding cattle and other ruminants. The disease is caused by the highly infectious Coxiella burnetii bacterium and, in addition to a reduced milk yield, it causes a wide range of reproduction issues, including miscarriages and the birth of weak calves.

This project aims to develop an inactivated vaccine exceeding existing options in terms of effectiveness and tolerability profile. As a result of the improvement and optimisation of existing vaccination strategies, morbidity



as well as the unspecific use of antibiotics and other drugs are reduced and the general performance of livestock is preserved, in addition to their health. As Q fever is a zoonotic disease, in addition to the improvement of animal health, this also helps to lower the risk of infection of humans through the reduced excretion of Coxiella in livestock.

The development of the novel inactivated vaccine is based on a technology for inactivating pathogens using low-energy electron irradiation, which was developed by Fraunhofer. The irradiation of the pathogens with low-energy electron beams damages the genetic information (nucleic acid) inside the pathogen; in contrast, the proteins and antigens on the surface remain largely intact for use in vaccines, while preventing the further reproduction of the pathogen. This provides the option for a more specific immune response and, hence, an improved vaccine. Moreover, the use of the Nine Mile Phase II strain of Coxiella burnetii ensures the faster and more cost-effective inactivation of the pathogen at lower biological safety levels (BSL 2 instead of BSL 3) compared with other available vaccines.

In addition to the technology for inactivating the pathogens, as part of the project, Fraunhofer IZI also contributes its infection biology expertise to the analysis, characterisation and quality assurance of the vaccine candidates.

Partners
University of Veterinary Medicine Hannover; Federal Research Institute for Animal Health, Friedrich-Loeffler-Institut (FLI); Wirtschafts-genossenschaft deutscher Tierärzte eG

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www.modern-vaccines-against-coxiella.de

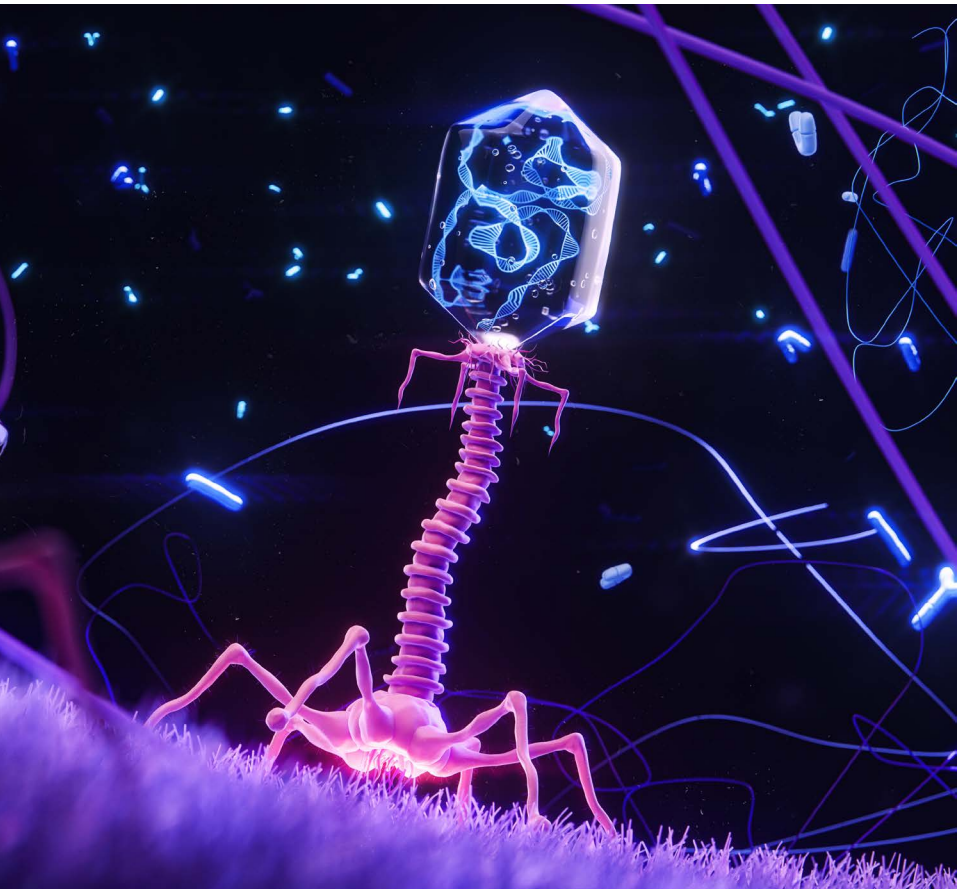
With support from

Federal Ministry of Food and Agriculture

by decision of the German Bundestag

Project manager

Federal Office for Agriculture and Food



Bacteriophages as an alternative to antibiotics

Increasing antibiotic resistance is a global health problem that is exacerbated by the overuse and inappropriate use of antibiotics. Bacteria are developing mechanisms to build resistance to these drugs, which impairs the effectiveness of conventional antibiotics. This leads to serious and difficult-to-treat bacterial infections, increased healthcare costs and a growing threat to public health. In addition to optimizing the use of antibiotics, there is a need to develop new classes of antibiotics and other antibacterial strategies.

Bacteriophages are an effective alternative for combating antibiotic-resistant bacteria.

These are viruses that infect and kill bacteria extremely specifically. Bacteriophages are almost ubiquitous in nature and play an essential role in the regulation of bacterial populations.

Phages consist of a nucleic acid core, either DNA or RNA, and surrounding coat proteins. They infect the bacterial cell by attaching to its surface and injecting their genome into the host cell. Within the bacterium, the bacteriophages multiply and produce enzymes that weaken the bacterial cell wall and finally destroy (lyse) the bacteria, releasing the newly formed phages to infect new bacteria.

Specificity and effectiveness make bacteriophages a potent alternative for the treatment of severe infections with antibiotic-resistant bacteria. At the Fraunhofer IZI, bacteriophages are systematically collected and examined for their medical potential. To this end, phages are isolated and characterized from a wide variety of environmental samples. In addition to the complete sequencing of the phage genome, it is examined, in particular, for resistance genes and potential virulence factors. The aim is to build a comprehensive therapeutic phage library, which will serve as a basis for the research and development of phage-based therapeutics.

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MELLIPA – LEEI inactivated parasites applied mucosally to treat allergies

Allergies have been increasing in the industrialized nations for decades. In this context, the decline in the number of parasite-borne infectious diseases is being discussed as a possible contributory factor. This hypothesis is based on similarities in the activation of the immune system. In allergic reactions, the immune system is wrongly activated by harmless environmental antigens and auto-antigens. This activation is specifically effected via Th2 immune cells, which, for example, stimulate antibody-producing B cells to produce IgE antibodies. These reactions largely correspond to those involved in the immune response to extracellular pathogens, such as parasites. In this case too, the immune system is activated via Th2 immune cells and IgE antibodies.

As a result, the permanent absence of parasitic infections might lead to a shift in the evolutionary balance between the Th1- and Th2-mediated immune responses and, as a result, to an errant immune response to harmless antigens.

In line with this theory, one therapeutic approach aims to re-establish the natural balance between the Th1- and Th2-mediated immune responses by administering parasitic antigens. However, the administration of active / living material is highly problematic in terms of safety, and difficult to justify as a treatment, even if the parasites are harmless to humans.

The MELLIPA project examines the suitability of inactivated parasites for allergy prevention. To achieve this, the parasites are inactivated using low energy electron inactivation (LEEI) and then formulated. Irradiation destroys the parasites' genetic material (DNA); however, it preserves the immunologically relevant surface materials. This ensures that the parasite preparation no longer has any infectious or pathogenic potential, while retaining a sufficient immunostimulatory effect. Its effectiveness is evaluated in an animal model (mouse) in which the drug is nasally applied via the mucous membrane.

The project focuses on the Toxoplasma gondii parasite whose native cellular material is highly active against various allergies and which is administered mucosally after LEEI inactivation.

Partners
Fraunhofer Institute for Toxicology and Experimental Medicine ITEM; Fraunhofer Institute for Translational Medicine and Pharmacology ITMP; Fraunhofer Institute for Applied Polymer Research IAP; Fraunhofer Institute for Electron Beam and Plasma Technology FEP; Fraunhofer Institute for Manufacturing Engineering and Automation IPA

Support
This project is financed as part of the Fraunhofer Cluster of Excellence for Immune-Mediated Diseases (CIMD).

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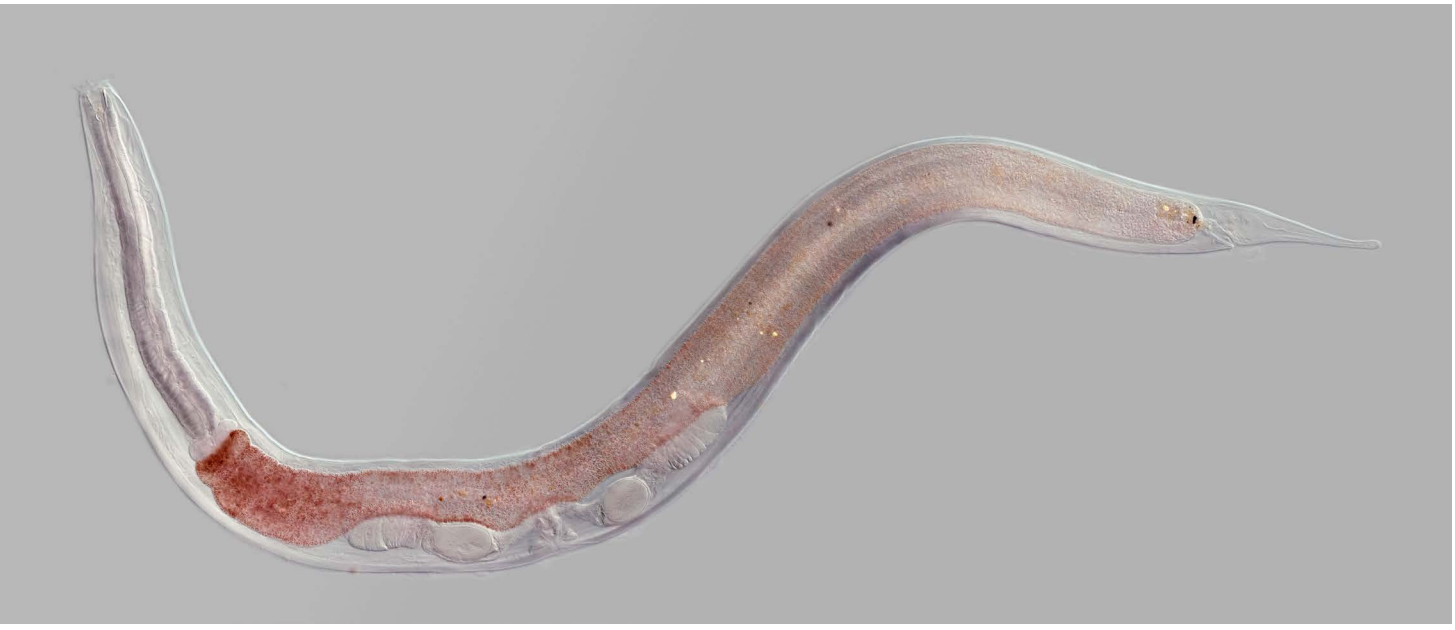

New strategies in the fight against the widespread disease periodontitis

Periodontitis is an inflammatory disease of the periodontium that can lead to destruction of tissue and bone around the teeth. The disease is caused by bacteria that settle in plaque and gum pockets and trigger an inflammatory response. If left untreated, this leads to damage to the entire periodontium and even tooth loss. Various studies also show a direct link between periodontitis and other diseases such as cardiovascular disease and diabetes, as well as an increased risk of stroke.

PerioTrap Pharmaceuticals GmbH, a Fraunhofer IZI spin-off, assumes the preclinical development of novel periodontitis treatments as part of the Paropaste project. The basis of the novel treatment concept is the inhibition of an enzyme that occurs almost exclusively in the bacteria that cause periodontitis and regulates the production of various virulence factors there. By selectively inhibiting these factors, the pathogenic germs can be specifically suppressed and the natural microbiome preserved. The use of classical antibiotics, on the other hand, leads to growth inhibition of all oral germs, which carries the risk of rapid and stronger recolonization by the pathogens.

The aim of the project is to test appropriate drug candidates for their efficacy and safety, thus creating the prerequisite for a clinical trial for initial testing in humans. The collaborative partners will address various regulatory aspects, including active ingredient formulation, tolerability, efficacy and toxicity.

Fraunhofer IZI will contribute its expertise in the development and validation of bioanalytical methods for the comprehensive characterization of small molecule drugs. In addition, toxicity and safety are being investigated both in vitro and in animal models as part of a GLP study.

This project is sponsored by the German Federal Ministry of Education and Research as part of its “KMU-Innovativ” program for small and medium-sized companies.

Partners
PerioTrap Pharmaceuticals GmbH; Skinomics GmbH; Fraunhofer Institute for Microstructure of Materials and Systems IMWS

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SPONSORED BY THE

Federal Ministry of Education and Research

EU project investigates links between land use change, biodiversity loss and zoonosis risk

Zoonosis Emergence
across Degraded and Restored
Forest Ecosystems

What influence do changes in land use and a loss of biodiversity have on the transmission of pathogens between animals and humans? This question is being investigated by an international and interdisciplinary research team as part of the EU project ZOE - »Zoonosis Emergence accros Degraded and Restored Forest Ecosystems«. Partners from seven European and four American countries are participating in the project, which is led by Charité - Universitätsmedizin Berlin. The Fraunhofer IZI is contributing its expertise in the field of virology and assay development.

Zoonoses are diseases that can be transmitted from animals to humans. Infection can occur through direct contact with animals, through contaminated food or through vectors such as ticks and mosquitoes. Humans play a decisive role in the development and spread of zoonoses. Agriculture and livestock farming, as well as the trade and consumption of wild animals, create environmental situations in which pathogens can easily be transmitted between animals and humans. Added to this are interventions in natural habitats, such as the clearing of forests to make room for livestock or plantations, or the expansion of urban areas.

The ZOE consortium intends to investigate the exact relationship between changes in land use, the loss of biodiversity and the risk of zoonoses. Partners from the fields of geography, geobotany, ecology, virology, immunology, epidemiology, sociology, psychology, anthropology and knowledge dissemination are working together on the project. One of the aims of the project is to carry out a detailed mapping of biodiversity in forest areas in which humans have intervened to varying degrees. To this end, researchers in Guatemala, Costa Rica, Slovenia and Slovakia study original forests as well as deforested and renaturalized areas.

In order to determine the prevailing land use and biodiversity, the nature of the landscape and the animal and plant species are recorded using satellite images and also directly on site. In addition, the scientists determine how many potentially dangerous microorganisms are circulating in the ecosystem by testing rodents, ticks and mosquitoes – as frequent carriers of zoonotic pathogens – for the presence of various bacteria and viruses using modern sequencing techniques.

At the Fraunhofer IZI, the team led by PD Dr. Sebastian Ulbert, Head of the Department of Infection Research and Diagnostics, develops assays to screen the samples from the study areas for all important groups of zoonotic pathogens. The samples mainly comprise blood samples from animals from the forest areas under investigation. In addition, blood samples from people living in the vicinity are examined in order to find out how many of the zoonotic pathogens have already been transmitted.

The research consortium "ZOE - Zoonosis Emergence accros Degraded and Restored Forest Ecosystems" is being funded by the European Union as part of "Horizon Europe", the EU Framework Program for Research and Innovation, with around four million euros over four years.

Partners
Charité – Universitätsmedizin Berlin, Germany; Leibniz University Hannover, Germany; Biomedical Research Center of the Slovak Academy of Sciences, Slovakia; Fraunhofer Institute for Cell Therapy and Immunology, Germany; Universidad del Valle de Guatemala, Guatemala; University of Vienna, Austria; University of Ljubljana, Slovenia; University of Potsdam, Germany; Pikado B.V., Netherlands; University of Costa Rica, Costa Rica; University of A Coruña, Spain; Aix-Marseille University, France; Protisvalor, France; National Autonomous University of Mexico, Mexico; Centro de Investigación y de Estudios Avanzados, Mexico; Wildlife Conservation Society, USA

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www.zoe-project.eu

Funded by
the European Union

Further selected projects

Studies on the interaction between the peroxisome proliferator-activated receptor γ (PPARγ) and the aryl hydrocarbon receptor (AhR) with regard to the mediation of anti-inflammatory effects and the maintenance of intestinal barrier integrity using different in vitro and in vivo models for chronic colitis

Since July 2023, Dr. Gustavo Henrique Oliveira da Rocha from São Paulo, Brazil, has been working on this ambitious topic at Fraunhofer IZI in the Preclinical Development and Validation department. This project is funded by a CAPES Humboldt Research Fellowship. This funding program was launched in 2013 by the Brazilian science funding organization CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior) and the Alexander von Humboldt Foundation. It enables above-average qualified scientists from Brazil who are at the beginning of their scientific careers to realize excellent project ideas at renowned research institutions in Germany. The project idea must therefore also be an optimal fit for the host institute and its expertise. In Germany, there are only a few institutions working with chronic inflammatory bowel disease (IBD) in applied research at the preclinical and clinical level. One of the main research topics of the department is the research and development of AhR agonists as promising new drugs for the therapy of IBD and the clinical translation of proprietary AhR ligands. Currently, there are no therapeutic options to cure IBD. Since the research results in this field to date show that AhR agonists can sustainably restore and maintain immunohomeostasis at the intestinal epithelial barrier, great hopes are being placed in the future clinical application of this new group of drugs.

Pharmacotherapy of IBD has long been concerned exclusively with effects in the intestine itself, while common extraintestinal manifestations that can lead to complications are usually ignored. Therefore, this project investigates the interaction of AhR ligands such as e.g.,

Alexander von HUMBOLDT STIFTUNG

CAPES

Indole-3-carbinol (I3C) or 2-(1H-indole-3-yl-carbonyl)-4-thiazolecarboxylic acid methyl ester (ITE) with PPARγ, in particular with regard to the mediation of anti-inflammatory effects in the intestine as well as in the intestine-associated and central nervous systems. AhR ligands have been studied as promising molecules for the treatment of IBD and related CNS complications, and PPARγ has been shown to be a key factor in the anti-inflammatory effects of both classical and novel IBD therapies. Therefore, this project aims to investigate the effect of I3C, ITE and three other proprietary synthetic AhR ligands on chemically (by dextran sulfate) or bacterially induced colitis and colitis-associated neuroinflammation in the intestine and periphery in clinically relevant chronic colitis models. In particular, it is important to investigate whether PPARγ plays a decisive role in downstream regulatory mechanisms in AhR activation. As a secondary goal, synergistic effects between AhR ligands and PPARγ-agonists will also be investigated. A first paper on this was already published in December 2024 (da Rocha et al. Int. J. Mol. Sci. 2024, 25, 13072. doi: 10.3390/ijms252313072.

Partners
Humboldt Foundation; CAPES

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Information on the CAPES Humboldt Research Fellowship:

www.humboldt-foundation.de/en/apply/sponsorship-programmes/capes-humboldt-research-fellowship

Systems Medicine Analyses for the Personalized Treatment of Bone Defects in Patients with Diabetes (SyMBoD)

Since 2019, the Department of Preclinical Development and Validation at Fraunhofer IZI has been working on the BMBF-funded SyMBoD project together with colleagues from Charité Berlin, the University of Hamburg, the University of Freiburg and Genevention GmbH from Göttingen. In an interdisciplinary approach, which combines animal models, clinical sampling, omics screening, bioinformatics, mathematical modelling and additive manufacturing of implants, possibilities for the personalized treatment of bone defects in patients with diabetes are to be explored. The tasks of the Department of Preclinical Development and Validation in the joint project include the molecular investigations of the collected (pre)clinical blood and bone samples, in particular by means of proteomics. With the help of these data and in collaboration with colleagues from the Institute for Computational Systems Biology at the University of Hamburg, it is possible to derive proteins, processes and signaling pathways involved that are disturbed in diabetes patients and lead to reduced bone regeneration. The targeted control of these processes by innovative functionalized bone implants can mean an improvement for the affected patients.

In order to achieve these goals, comprehensive quantitative protein profiles must be measured. However, bone tissue in particular poses a particular challenge for proteomic analysis, as it is very compact and mineralized and consists mainly of collagens. To enable measuring non-collagen, low-abundant, regulating proteins, the processing and measurement methods must be optimized in a targeted manner. In the course of the SyMBoD project, an innovative two-step processing combining acid- and chaotrope-based protein extraction was developed. The established workflow allows a comprehensive and reproducible screening of more than 4,000 proteins (Wiltzsch et al. J Proteome Res., under review). This depth of analysis allows conclusions to be drawn about the dysregulation of individual signaling pathways and cell

populations. For example, it was possible to uncover that certain immune cell populations occur more frequently in the regenerated tissue of diabetic animal models and have a negative influence on healing there. Ongoing intervention studies are intended to clarify whether the targeted influence of these populations can improve bone regeneration.

Another challenge of the project was the integration of the large amounts of data obtained. Hundreds of dysregulated proteins and processes can be derived from the proteomic profiles obtained. However, it is not easy to determine which are relevant and should be prioritized in bone healing. To support this, a meta-study was carried out as part of the project. In this study, 31 published proteomic datasets were reanalyzed in a specially developed bioinformatics pipeline. The datasets included different species and biological hierarchies – from cell cultures to tissues to systemic approaches. With the help of the developed pipeline, data harmonization across studies, the selection and prioritization of participating proteins and digital drug repurposing were carried out. In doing so, 51 proteins and their involved processes could be identified, which are universally involved in bone healing. Among these are proteins that are known in connection with bone regeneration, e.g., collagens, fibronectin and periostin. However, the study also identified nine potential biomarkers that can predict the course of bone healing. In addition, eight bioactive proteins could be proposed. These will be available in the future as innovative, healing-promoting implant functionalizations. Through an integrated drug repurposing approach, four approved drugs could be identified that could potentially promote bone healing. All results of the study were published in 2024 (Schmidt et al. J Tissue Eng, 2024, doi: 10.1177/20417314241295332).

In a third aspect of the SyMBoD project, together with the research group of Prof. Sara Checa from the Julius Wolff Institute of the Charité Berlin, it was investigated whether a prediction of scaffold-assisted bone regeneration is possible by combining mechanical and serum proteomics data. The OMIBONE program was developed for this purpose. This first uses the processing of proteome data from the Ingenuity Pathway Analysis (IPA) software to link differentially abundant proteins with changes to the underlying biological processes. This metadata is used to simulate the progress of bone regeneration in a time-resolved manner. The comparison with experimental data showed that a personalized prediction of bone healing is possible for defined fracture fixations as well as for diseases that impair regeneration (Jaber et al. Bone 2025, doi: 10.1016/j.bone.2024.117288).

Partners
Charité - Universitätsmedizin Berlin; University of Hamburg; University of Freiburg; Genevention GmbH

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Federal Ministry of Education and Research

An allogenic cell treatment product for treating focal condral defects in the knee – Production of clinical test products for a phase I/IIa clinical study

The "MesemCart" product developed by BIONCaRT GmbH (formerly BioPlanta GmbH) is based on mesenchymal stromal cells and will be used to treat acute and chronic cartilage damage in the knee joint. The cells harvested from umbilical cord blood activate regenerative processes and help to restore hyaline cartilage. This novel treatment aims to repair the cartilage, alleviate pain, improve mobility and reduce arthrosis symptoms in the knee.

As part of the joint project, a clinical (phase I/IIa) study is to be carried out to verify the safety of the treatment. Fraunhofer IZI's part of the project will provide the test products for the planned clinical studies.

Among other aspects, this includes the aseptic production, formulation and filling of the test products based on a cryopreserved cellular intermediate product which is to be produced by a contract manufacturing organisation. Furthermore, this part of the project also includes the execution of all release-relevant quality inspections of the final product, as well as packaging and preparation for shipping to the clinical test centres.

In a previous project, the scientific and technological preconditions for the pharmaceutical production of the clinical test products were established and an update of the product list was obtained under the current manufacturing permit of Fraunhofer IZI in accordance with section 13 of the German Medicines Law. In addition, the product has already undergone numerous tests at GLP conditions in the Fraunhofer IZI GLP test facility. These involved checking for undesirable biodistribution and tumorigenicity.

Partners
BIONCaRT GmbH (formerly BioPlanta GmbH); Dresden Technical University | University Centre of Orthopaedics, Trauma and Plastic Surgery; Dresden Coordination Centre for Clinical Studies

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Micro-clots as predictive parameters of vascular and neurodegenerative brain changes in old age

Micro-clots are tiny blood clots of fibrin, blood platelets and other coagulation factors which develop in the smaller blood vessels. They are caused by excessive activation of the coagulation system, often as a result of inflammation, an infection, or other stress-related conditions of the body. These tiny blood clots can circulate in the small blood vessels and become stuck, which obstructs the blood flow in the capillaries or micro-vessels and can cause serious health issues.

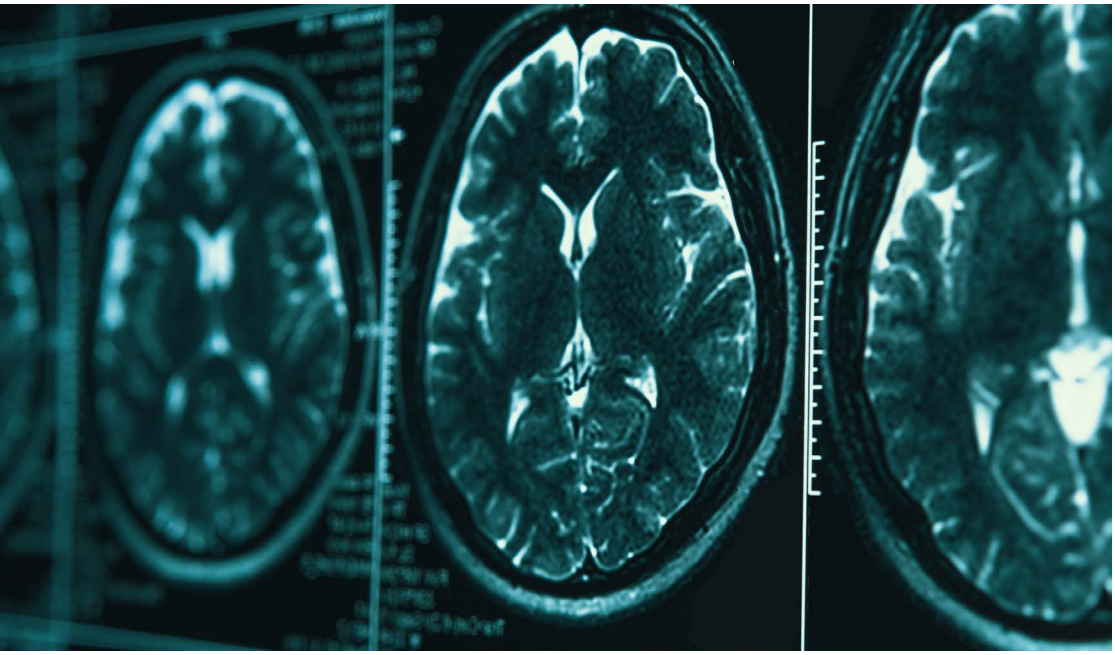
This project aims to examine the connection between the presence of micro-clots (or their concentrations) and brain health. To this end, the number and composition of micro-clots in clinical samples is to be analyzed and associated with other clinical data. The focus is on examining a potential connection between the concentration of micro-clots in the blood and cognition parameters, as well as with brain structure and functioning, which is to be specified further by including MRT parameters. The study is based on samples

Gefördert aus Mitteln der Europäischen Union

Europa fördert Sachsen.
EFRE
Europäischer Fonds für regionale Entwicklung

Freistaat Sachsen

This project is co-financed by tax revenues on the basis of the budget approved by members of the Saxon state parliament.



from the LIFE Adult studies at the Leipzig Medical Biobank of the Leipzig Faculty of Medicine.

High-throughput detection and quantification of micro-clots in the blood of the selected cohort are examined at Fraunhofer IZI using real-time deformability cytometry (RT-DC).

Partners
Leipzig Faculty of Medicine, Leipzig Research Centre for Lifestyle Diseases (LIFE); Max Planck Institute for Human Cognitive and Brain Sciences Leipzig

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Gefördert aus Mitteln der Europäischen Union

Europa fördert Sachsen.
EFRE
Europäischer Fonds für regionale Entwicklung

MIRA – Development of a sustainable molecular-diagnostic test platform for cervical cancer screening

Around 75 % of all cervical cancer cases are caused by the human papilloma virus. Vaccines are available to prevent this; however, these are not used comprehensively. In addition, the vaccination is only effective provided there was no prior persistent infection. This means a fast, effective and reliable test could help healthcare systems to stratify the persons to be vaccinated and, on the other hand, it could increase awareness of the need for screenings which facilitate the earlier detection of infections and cancers and can improve the success rate in treatment.

This project aims to develop a point-of-care test which takes up sample material and releases the nucleic acids of the viral pathogens. These are replicated via isothermal amplification with the required temperature being achieved and maintained with the help of an exothermic chemical reaction. Afterwards, the result of the detection reaction can simply be read off. Moreover, the cartridge is to be made of a sustainable material which, in turn, is manufactured from renewable raw materials and is compostable.

Fraunhofer IZI contributes its expertise in sample processing and the development of molecular biological rapid tests.

Through its gynecology clinic, Leipzig University Hospital will become involved in the project as a clinical partner on the basis of a subcontract. In addition to medical expertise, it will also contribute clinical samples of patients with an HPV infection in order to evaluate the functionality of the system in a proof-of-concept study.

Partners
INTU Diagnostics GmbH (coordination); VOXDALE GmbH; Leipzig University Hospital Leipzig AöR; Institut für Molekulare Diagnostik und Bioanalytik (IMDB) gGmbH

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The impact of human endogenous retroviruses on autoimmune and tumor diseases

Around 8 % of the human genome consist of human endogenous retroviruses (HERV). These sequences come from infectious retroviruses that have become permanently integrated into the human genome as part of evolution. Most of these HERV are inactive or have mutated so that their ability to replicate is impaired. However, some HERV have retained functional elements and can, therefore, be involved in certain physiological and immunological processes. For example, HERV are connected to various autoimmune disorders, neurodegenerative diseases and cancers.

HERV (or proteins expressed by them) provide interesting target structures for treating autoimmune diseases and cancer. On the one hand, this is because certain proteins are directly involved in tumor biology. Others are exclusively produced by cancer cells and presented on its surface, making them specific targets for antibodies, active agents or immunotherapies.

At Fraunhofer IZI, envelope proteins of endogenous retroviruses of the HERV-K class, in particular, are tested for their suitability as tumor markers and therapeutic targets. To this end, monoclonal antibodies against HERV-K envelope proteins are being developed and various tumor entities are being tested for their expression. These research activities aim to evaluate antibodies for pre-clinical and clinical development and to render them usable for tumor-specific treatment.

Another focus of research examines immunomodulation in pathophysiological processes of multiple sclerosis (MS). Various HERV proteins are attributed as having immuno-stimulating and neurotoxic characteristics which can contribute to the development of MS.

This project is financed with support from the state of Saxony-Anhalt.

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Europa fördert Sachsen.
EFRE
Europäischer Fonds für regionale Entwicklung

ADsorb – Development of an implantable system for liquorpheresis in neurological diseases using the example of Alzheimer's dementia

At the present time, Alzheimer's dementia (AD) is one of the biggest medical challenges in our society. So far, this disease can neither be cured nor can its progression be halted effectively.

The accumulation of intracerebral beta-amyloid within the central nervous system (CNS) and the cerebrospinal fluid correlates with the characteristic symptoms, such as memory loss and, in part, pronounced behavioral changes. Therefore, the reduction of this neurotoxic protein through liquorpheresis appears a promising therapeutic approach. This approach is based on extracorporeal blood purification therapies which are used, in particular, to treat acute and chronic renal and liver failure as well as autoimmune disorders. These methods are based on the targeted reduction of pathogenic molecules which would otherwise accumulate in tissues and contribute to the progression of the illness. In this context, liquorpheresis could help to balance the age- or illness-related dysfunction of the liquor system and, as a result, to slow down and, in the best case, stop the progression of the illness.

The project aims to develop and research a liquorpheresis technology for the removal of specific target proteins which are generated in the CNS from the cerebrospinal fluid. To this end, a model system will initially be developed in the transgenic Alzheimer's mouse to try out a miniaturized, implantable liquorpheresis device. Fraunhofer IZI will contribute its expertise in the field of extracorporeal technologies and adsorbers.

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Partners
Rostock University Medical Center; University of Rostock

Support
Go-Bio initial program / Federal Ministry of Education and Research

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and Research

EU and joint projects

AIDPATH – AI powered, Decentralized Production for Advanced Therapies in the Hospital

The AIDPATH EU project brings partners from industry and research together to develop an automated, smart system which can produce targeted and personalized cell therapy directly at the place of treatment, i.e. in the hospital. In addition, the project also looks into the integration of the system into the hospital environment under consideration of the logistics processes and of data management and security. Fraunhofer IZI is contributing its expertise, in particular, in the automation of production processes and plant networking, to the project.

- Coordination: Fraunhofer Institute for Production Technology IPT
- Project management at Fraunhofer IZI: Dr. Paul Franz
- Funding: EU / Horizon Europe

Further information can be found on page 37.

www.sciencrew.com/c/6499?title=AIDPATH

CERTAINTY – Cellular immunoTherapy Avatar for personalized cancer treatment

A team of 18 partners (led by Fraunhofer IZI) is planning to develop a virtual twin to improve treatment with personalized cancer immuno-therapies in future in the framework of the CERTAINTY project. As an example, the virtual twin will initially be implemented for multiple myeloma (MM), a malignant bone marrow disorder. It is designed to comprehensively represent the individual pathophysiology of patients who are candidates for cellular immune-therapies or are undergoing such. In this case, the Fraunhofer IZI team contributes its expertise in the field of personalized medicine and molecular diagnostics.

- Coordination: Fraunhofer IZI
- Project management at Fraunhofer IZI: Dr. Kristin Reiche
- Funding: EU / Horizon Europe

www.certainty-virtualtwin.eu

CREATIC – Central European Advanced Therapy and Immunotherapy Centre

In the framework of the CREATIC project, the EU supports the development of a new research and development center for novel treatments at the Masaryk University in Brno, Czech Republic. This project aims to develop research and innovation in the field of cell and gene therapy into clinical practice for the patients' benefit. The CREATIC research focuses on rare illnesses, including both rare hereditary diseases and various rare cancers. Fraunhofer IZI provides advice and training in the field of GMP process development and the production of advanced therapy medicinal products (ATMPs). Additionally, Fraunhofer IZI is also involved in shared pilot projects in which cells are to be developed for immuno-therapies (e.g., CAR-NK cells and CAR macrophages).

- Coordination: Masaryk University
- Project management at Fraunhofer IZI: Ilka Henze
- Funding: EU / Horizon Europe

www.creatic.muni.cz

ImSavar – Nonclinical mimicking of the immune system effects of immuno-modulatory therapies

The EU consortium imSAVAR is designed to lay the foundation for new, Europe-wide standards in the development of medication. Its 28 international partners from eleven countries aim to improve existing model systems and to develop new ones to identify undesired side effects of new treatments on the immune system. As part of this, new bio-markers for diagnosing and assessing immune-mediated pharmacologies and toxicities are to be developed. In addition, research into toxicity mechanisms and the potential for reducing such through therapeutic measures is to be carried out.

- Coordination: Fraunhofer IZI / Novartis AG
- Project management at Fraunhofer IZI: Dr. Kristin Reiche
- Funding: EU / IMI

www.imsavar.eu

ISOS – Implantable Ecosystems of Genetically Modified Bacteria for the Personalized Treatment of Patients with Chronic Diseases

ISOS focuses its research on the treatment of chronic diseases requiring prolonged treatment. This project aims to develop a bio-medical product for the in-situ production and automatic administration of therapeutic agents into which a complex eco-system of probiotic, genetically engineered bacteria (GEB) is integrated for the first time. In this case, a bio-reactor based on biomaterials provides the GEB eco-system. The design and configuration of the GEB eco-system are customized for the specific patient with the help of in-silico tools and synthetic biology. As a result, ISOS is designed to establish the basis for a new generation of therapeutic products.

- Coordination: SILK BIOMED, S.L.
- Project management at Fraunhofer IZI: Prof. Dr. Stefan Kalkhof
- Funding: EIC Pathfinder open

JOIN4ATMP – Map, join and drive European activities for advanced therapy medicinal product development and implementation for patient and society benefit

JOIN4ATMP is to contribute to accelerating the development and broad availability of novel treatments in Europe. Since the standardized, conventional regulatory requirements for drug approval cannot be directly transferred to complex gene and cell therapies, obstacles in the application and development of advanced therapy medicinal products (ATMPs) are to be identified and, if possible, standardized solutions developed to overcome these. The European University Hospital Alliance, the T2EVOLVE consortium and the RESTORE initiative are involved in this project. They are supported by industrial partners and patient advocacy groups, in addition to other partners from ATMP development, production, application and regulation.

- Coordination: Charité – Universitätsmedizin Berlin
- Project management at Fraunhofer IZI: Dr. Ulrich Blache
- Funding: EU / Horizon Europe

https://join4atmp.eu

REANIMA – Prevent heart failure by reawakening the endogenous regenerative ability of the mammalian heart

REANIMA aims to provide new treatments for heart regeneration. It is the first project in Europe in this field to include results from basic research with the aim of transferring these into medical application. The knowledge obtained in animal models is to be analyzed comprehensively to develop new regenerative treatments of cardiac insufficiency. Twelve European partners are involved in the project.

- Coordination: Spanish National Center for Cardiovascular Research
- Project management at Fraunhofer IZI: Dr. Paul Franz
- Funding: EU / Horizon Europe

www.reanima2020.eu

REMEDI4ALL – European Platform for Medicines Repurposing

In the REMEDi4ALL research initiative, 24 project partners want to promote the repurposing of medication, i.e., the search for new therapeutic applications for existing medications, in fields with a high and unmet medical need. Fraunhofer IZI is evaluating known drug candidates identified as being interesting in the repurposing project in an in vivo animal model. As part of this, a technology platform is to be developed for evaluating approved medication from the identification of new fields of application through in vitro and in vivo testing as well as in clinical examinations in the future.

- Coordination: EATRIS ERIC
- Project management at Fraunhofer IZI: PD Dr. Thomas Grunwald
- Funding: EU / Horizon Europe

www.remedi4all.org

T2Evolve – Accelerating Development and increasing awareness and access of patients with cancer to immunothrapy

T2EVOLVE aims to accelerate the CAR-T cell treatment development within the EU, expand patient access to this treatment and, concurrently, provide guidelines for the sustainable introduction of this cancer treatment in the EU healthcare system. Additionally, the 27 partners from nine European countries want to reduce the financial burden which healthcare systems place on the economy and society. Also, by including patients, the project ensures that the focus in both research and treatment takes account of the perspective of cancer patients.

- Coordination: University Hospital Würzburg
- Project management at Fraunhofer IZI: Dr. Kristin Reiche & Dr. Paul Franz
- Funding: EU / IMI

www.t2evolve.com

ZOE – Zoonoses Emergence across Degraded and Restored Forest Ecosystems

In ZOE, 16 partners from 7 European and 4 American countries examine the impact of changes in land use and loss of biological diversity on the transmission of pathogens between animals and humans. The project, as an example, includes detailed biodiversity mapping of forest areas with different levels of human intervention. For this, researchers in Guatemala, Costa Rica, Slovenia and Slovakia will study both virgin forests as well as deforested and renaturalized areas. Fraunhofer IZI is contributing its expertise in the fields of virology and assay development.

- Coordination: Charité – Universitätsmedizin Berlin
- Project management at Fraunhofer IZI: PD Dr. Sebastian Ulbert
- Funding: EU / Horizon Europe

Further information can be found on page 46.

www.zoe-project.eu

RNAuto – Automated production of mRNA-based vaccines and gene therapeutics

In the RNAuto cooperative project, seven Fraunhofer institutes are working to develop automated production technologies for mRNA-based drugs.

mRNA-based vaccines as well as gene and cell therapeutics are innovative drugs with which infectious and genetic diseases and cancer can be prevented or treated. To ensure cost efficiency and availability in view of growing demand, automated and digitally supported production technologies are needed to ensure the fast, safe and reliable production of mRNA-based drugs.

The project focuses on the development of bioprocesses and production technologies for the modular and automated mRNA, mRNA nano carrier and mRNA-modified cell production, which can be ramped up to industrial scale.

This project brings together the expertise of different Fraunhofer institutes from the fields of vaccine development, cell and gene therapy, bioprocess development, smart sensor technology, automation and digitalization of production methods.

- Coordination: Fraunhofer IZI
- Funding: Fraunhofer

https://s.fhg.de/rnauto

SaxoCell – Precision medicine by cell and gene therapies

SaxoCell stands for the development of new fields of application and production methods for gene and cell therapeutics, so-called “living drugs”. Here, the aim is to produce cells with precisely defined functions and a high safety profile for safe, clinical application on an industrial scale and at socially acceptable costs to permit a realistic and feasible business model with a high value creation potential for Saxony. In the SaxoCell cluster, Fraunhofer IZI is cooperating with TU Dresden, Leipzig University and the Chemnitz hospital. Fraunhofer IZI contributes its competences in the field of cell technology focusing, in particular, on the development and production of genetically engineered immune cells (e.g., CAR-NK cells and CAR-T cells). Moreover, pharmaceutical production processes are being developed and established, while cell and molecular biological datasets are collected and bio-statistically evaluated on the SaxoCellOmics technology platform.

- Coordination: Fraunhofer IZI / TU Dresden
- Funding: BMBF / Clusters for Future

Further information can be found on pages 38 f.

www.saxocell.de

WIR! sind DIANA – Technologies for future point of care diagnostics

Since 2021, Fraunhofer IZI and the Fraunhofer Institute for Machine Tools and Forming Technology (IWU) have coordinated the "WIR! sind DIANA" alliance under the BMBF funding program "WIR! – Wandel durch Innovation in der Region". The alliance is pursuing the key task of developing the region in central and western Saxony as well as eastern Thuringia into an innovation and competence leader for point-of-care technologies in Germany. As a result, in the medium term, this regional and innovative initiative for the development of medical high-technology products is to also form the basis for new jobs in the region. Besides the coordinating Fraunhofer institutes, supra-regional partners are also part of the alliance. To put this project on a more permanent basis, DIANA – Point-of-Care-Technologien Mitteldeutschland e.V., a registered association, was set up in December 2023.

- Coordination: Fraunhofer IZI / Fraunhofer IWU
- Funding: BMBF

www.wirsinddiana.de

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