Fraunhofer

IZI

FRAUNHOFER INSTITUTE FOR CELL THERAPY AND IMMUNOLOGY IZI

ANNUAL REPORT 2012

ANNUAL REPORT
2012

Cover picture

Winner of the 2012 "Fascination Microcosmos" photo competition.

Title: Cells seeking contact

Name: Dr. Mike Francke

Institution: Translational Center for Regenerative Medicine (TRM) at the University of Leipzig

Type of microscopy: Laser scanning microscopy

Object: Retinal glial cell (Müller cell)

DIRECTOR

2012 was a major year for the Fraunhofer-Gesellschaft, shaped by the transfer of the organization's presidency from Professor Hans-Jörg Bullinger to Professor Raimund Neugebauer. The organization is extremely thankful to Professor Bullinger for his ten years of commitment, in which he continued to drive forward Fraunhofer's concept for success. As a Saxon Fraunhofer institute we are, of course, extremely pleased that with the appointment of Professor Neugebauer, a former institute director from the Free State of Saxony has been elected to Fraunhofer president. In the early 90s, he established a large Fraunhofer institute, the Institute for Machine Tools and Forming Technology, in Chemnitz. Not only did he demonstrate a remarkable amount of energy in doing this, but he also led the institute to international success.

The support that we receive from the Free State of Saxony and the City of Leipzig is associated with the understandable desire not only to take on innovative research topics and gain internationally respected knowledge, but also to provide for an increasing number of valuable jobs and the influx of highly educated young professionals, besides also making a significant contribution to the development of the local region by founding new companies.

As we are well aware, there are still not enough small and medium-sized technology companies in the former eastern German states which are able to compete on an international level. In this respect, founding new companies is a pressing political goal which we also recognize and pursue. Spin-off companies give entrepreneurial colleagues the opportunity to put their ideas and concepts into practice. Since being established, the Fraunhofer IZI has experienced four such spin-offs and has also been responsible for establishing seven companies, and helping them to get started up. These include five subsidiaries of international companies, whose move to BIO CITY Leipzig stems from successful cooperation projects with the Fraunhofer IZI.

In the 2012 reporting period we were also able to attract substantial major projects, many of which with international partners. For example, we are involved in two projects with the Translational Centre for Regenerative Medicine at the University of Leipzig, which set out to investigate aspects of cell therapy treatment and cell migration in connection with ischemia and stroke. International partners are involved in both projects, e. g. the Californian Stanford University and the University of Eastern Finland. On behalf of a Canadian company and in cooperation with its Leipzig subsidiary, we are qualifying and supporting the company's extremely innovative drug platform and its use for the treatment of inflammatory diseases. After obtaining approval to set up a new unit as part of the Fraunhofer Attract program, the so-called DNA origami technique will be developed further at the Fraunhofer IZI from the start of 2013 with a view to its commercial applicability.

We place great importance on international cooperations as they allow us to expand our business portfolio and find new partners. This is why the cooperation work undertaken with our Korean partners has been further developed, with many young colleagues having already taken part in the exchange. We are now aiming to establish a communal laboratory at Hwasun Hospital – the university hospital at Chonnam National University – where specific areas of project work are planned to be expanded upon. We also strengthened our relationships with two prestigious university locations in the Canadian provinces of Quebec and Ontario. With regard to both South Korea and Canada, we were pleased to note that the cooperations are being met with broad support, not only from research partners, but also from political authorities.

Life in and around the Fraunhofer IZI in 2012 was still very much characterized by the construction of our first extension building. The majority of the building works could be completed by the end of the year and were gradually cleared for acceptance. The building opens up a bottleneck with respect to clean rooms geared towards the development of cell technology under the highest pharmaceutical standards and allows us to conduct experimental work in system-related cell biology and biomedicine. Our equipment portfolio for highly developed imaging will also be complemented by a 7-tesla small animal MRI system. Even as the building work was being completed it became clear that the capacities gained through the extension still remained insufficient and further additions would be required. To this end, numerous talks have been held throughout the entire year with the Free State of Saxony, the City of Leipzig and the Fraunhofer-Gesellschaft, which have paved the way for a second extension building: Construction is set to begin in 2013.

In the 2011 annual report I expressed my desire for 2012 to be Fraunhofer IZI's most successful year. I'm now happy to confirm that this was, indeed, the case. For the first time, in the previous year already, we were able to lay down our financial targets for 2013 not only conceptually but also in a legally binding manner, as agreed between the Fraunhofer-Gesellschaft and the board of trustees, with our partners and clients. Our colleagues should be very proud of themselves – we couldn't have done this without their successful work.

Also in 2012, the institute maintained scientific exchanges by organizing and being involved in various conferences and symposiums. For example, members of staff at the Fraunhofer IZI were largely responsible for organizing and structuring the "7th International Symposium on Neuroprotection and Neurorepair" in Potsdam and the 7th annual conference of the German Society for Regenerative Medicine in Leipzig. Preparations for the approaching World Conference on Regenerative Medicine, which will be held from 23–25 October in Leipzig, have also been long under way. The conference is expected to attract around 1,000 international attendees from various research disciplines to Leipzig.

To conclude, I would again like to show my appreciation for all of our sponsors, partners and, not least, members of staff at the institute. We look forward to seeing what new challenges 2013 brings with well-founded optimism.

Prof. Dr. Frank Emmrich

HIGHLIGHTS 2012

QUALITY PAYS OFF

The Fraunhofer IZI is initiating substantial follow-up projects with a Canadian and an Australian company, as well as with their European branches.

Chronic inflammatory diseases, particularly affecting the respiratory tract, often very severely impair the quality of life of those affected and also place a significant burden on the healthcare system. Approximately 300 million people around the world suffer from asthma, 600 million from chronic obstructive pulmonary disease (COPD) and up to 30 per cent of the population suffers from allergic rhinitis. Chronic inflammatory diseases of the intestine (e. g. ulcerative colitis) and of the joints (e. g. rheumatoid arthritis) are also common. Glucocorticoids are central to various therapeutic strategies, however they are also associated with a number of side effects.

Nuvo Research GmbH, Fraunhofer IZI and the Translational Centre for Regenerative Medicine at the University of Leipzig have joined forces to research and develop an innovative drug platform which will support the quicker development of new drugs for various types of chronic inflammatory diseases.

The project, valued at a total of 6.3 million euros, is being funded through the Sächsische Aufbaubank (Saxon Development Bank) with a total of 4.4 million euros coming from the European Regional Development Fund (ERDF) and also from the Free State of Saxony. The project is based on a previous project in which a promising active ingredient candidate was tested with regard to safety and efficacy in the area of inflammatory diseases and was further developed at the Fraunhofer IZI.

The data obtained from this project were so encouraging that a whole series of active ingredients are to be developed in future for various applications on the basis of this active ingredient. The low-molecular base active ingredient modulates the immune system and controls inflammatory processes, causing significantly fewer side effects than previous active ingredients. This therefore opens up numerous areas of application in the field of inflammatory diseases.

A further follow-up project was developed together with Prima BioMed GmbH and has been authorized by the Sächsische Aufbaubank (Saxon Development Bank, SAB) and the Saxon State Ministry for Science and the Arts (SMWK) to begin implementing measures ahead of schedule. This project involves the clinical investigation of a new form of therapy based on dendritic cells for the treatment of ovarian cancer and is valued at a total of 6.5 million euros.

COMPLETION OF THE FIRST EXTENSION BUILDING

Good things come to those who wait. The foundation stone for the first extension building was laid back in September 2009. In October 2012, the time had finally come: The new build was ready for its technical handover. The complicated building requirements led to a time-intensive construction phase. In future, new therapy concepts can now be developed and tested over 1,200 m² of additional laboratory space.

Until now, the Ischemia Research, Clinic-oriented Therapy Assessment and Experimental Imaging Units had still been operating from laboratories at the University of Leipzig. The move thus signifies the long awaited incorporation of these units into the day-to-day workings of the institute. Colleagues who previously felt more like guests at their own institute will now appreciate the closer proximity, more intensive communication and, not least, the company cafeteria more than ever before.

Laboratories for experimental medicine are located on the ground floor, where new forms of therapy for the treatment of neurodegenerative diseases such as stroke will be developed and tested with the aid of small and large animal models. Laboratory capacities on the first floor are kitted out for work in the fields of molecular and cell biology. The modern research infrastructure is complemented by imaging technologies such as laser scanning microscopy, bioluminescence imaging and a 7-tesla small animal MRI system.

The second floor houses the building maintenance center for the technically sophisticated new build which looks after the construction's ventilation and heating. The third floor is home to another 450 m² clean room facility used by the Cell Engineering / GMP Unit. This is connected via a bridge to BIO CITY Leipzig, where the unit already has a 450 m² clean room facility. Both facilities are designed for the GMP-compliant manufacture of cell therapeutic preparations for clinical trials. The existing facility was working to full capacity, meaning no additional projects could be taken on in this area; the extension was therefore urgently required.

A celebration was held to mark the opening of the first extension building on 23 January 2013. With welcoming speeches given by Stanislav Tillich, Minister-President of Saxony, and Mayor Burkhard Jung, the institute's staff were wished every success as they now fill the "daughter cell" with life.

There was also cause for celebration when it was announced that the third construction phase is scheduled to begin as early as 2013. But more on that in the next annual report.

7TH FRAUNHOFER LIFE SCIENCE SYMPOSIUM IN CONNECTION WITH THE ANNUAL CONFERENCE OF THE GERMAN SOCIETY FOR STEM CELL RESEARCH

Since 2006, the Fraunhofer IZI has organized the Fraunhofer Life Science Symposium Leipzig on an annual basis, each year focusing on a different topic from biomedical research. The spotlight in 2012 was on new findings from the field of stem cell research.

This year, stem cells and their clinical application formed the symposium's key topics. Stem cell research opens up new channels for medical applications, especially in the treatment of degenerative diseases. More and more research projects are approaching the stage of clinical use; at the same time, they promise to deliver solutions to issues arising from demographic change. This year, it was only logical that the symposium was linked to the annual conference of the German Society for Stem Cell Research (GSZ). The GSZ unites German stem cell researchers with the aim of promoting scientific exchange.

As in previous years, the conference was held towards the end of the year from 29–30 November at the Fraunhofer IZI. With a record number of nearly 230 participants, the event was already fully-booked four weeks before taking place.

The two-day program packed in a wealth of content: A total of 40 presentations on various aspects of stem cell research provided plenty of talking points. Furthermore, a total of 80 additional research works were presented in two poster sessions. A comprehensive industry exhibition and presentations enabled 22 companies to present new products in the field of stem cell research. This gave rise to active exchanges between attendees with research, clinical and industry backgrounds, not only during sessions but also in breaks and beyond.

Topics under discussion ranged from fundamental ways of developing stem cells for the most diverse therapeutic and diagnostic applications to application-related research which aims to develop specific therapy concepts, e. g. for diseases affecting the musculoskeletal system or nervous system.

The recognition and distinction of the work conducted by Professor Anna Wobus from Gatersleben was a special highlight. Following an extremely interesting presentation which provided an overview of the development of stem cell research in Germany, Professor Wobus was honored with an award by the German Society for Stem Cell Research for her personal achievements in this field. She was also made honorary member of the GSZ.

The next Fraunhofer Life Science Symposium will once again take place as part of the World Conference on Regenerative Medicine from 23–25 October 2013 in Leipzig.

STRUCTURES AND NUMBERS

PORTRAIT OF THE INSTITUTE

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

Over the past years, biotechnology and regenerative medicine have taken on greater significance. Of these specialized fields the public expects new therapies for the treatment of diseases which lead to the irreversible damage of tissue and organs; these invariable include chronic, autoimmune and tumor diseases.

The goal is to systematically repair the damages caused by diseases associated with the destruction of cells or tissue and to correct dysfunctions by means of cell therapies, tissue engineering or targeted modulation of the immune system. This goal can be achieved by stimulating the body's own regeneration processes or by means of biological substitutes in form of extracorporeally cultivated tissues.

General topic: Cell therapy and immunology

In the narrow sense of the word, cell therapy denotes the transfer of cells that provide a substitute for lost functions however are also capable of taking over advanced active functions and additionally the term describes the repairing of defects by means of treatment with cells. Stem cells can be transferred in order to induce the formation or repair of tissue.

This builds a bridge to immunology, which is concerned with cellular defense and control mechanisms. It is expected that cell therapeutic methods for targeted enhancement, suppression or regeneration of the immune system will soon be available, e. g. for stimulating the defense mechanisms of degenerate cells or for suppressing undesired graft-versus-host reactions against grafted tissue. In addition, the further development of immunomodulatory techniques, e. g. vaccination, is of particular importance.

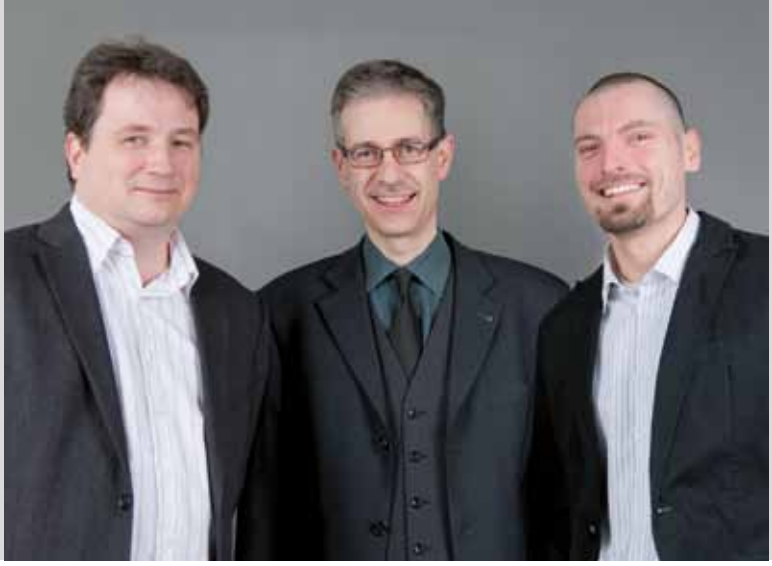
The institute's tasks

The institute comprises the four departments of Cell Engineering, Immunology, Cell Therapy and Diagnostics. Assigned to these departments are a total of 17 units having a broad spectrum of competencies and qualifications.

The institute's spectrum of services is aimed at specific problem solutions at the interfaces of medicine, biosciences and engineering.

With this, the Fraunhofer IZI addresses not only the biomedical industry, including pharmaceutical and bio-technological companies and diagnostic laboratories, but also hospitals and research facilities.

The core competencies are concentrated in the field of regenerative medicine, which in addition to the development and testing of new agents also specifically includes cell therapeutic approaches to the regeneration of dysfunctional tissues and organs through to biological replacement with tissues cultivated in vitro (tissue engineering). For an unproblematic engraftment of these tissues it is necessary to detect cellular and immunological mechanisms of defense and control and to integrate them into the development of methods and products. Around these core competencies a large variety of tasks for new products and methods arises. The institute is strongly oriented towards the hospitals and takes on quality testing, the production of clinical test samples according to GMP guidelines and contracted clinical trials. In addition, we support our partners in obtaining manufacturing and marketing authorizations.



ORGANIZATION

The institute comprises four departments which are organized into different units. Scientific services are supported by the administration and the executive departments "Business Development and Patent Management" and "Press and Public Affairs".

Business Development and Patent Management

The Fraunhofer IZI considers itself to be a professional service provider in the field of research and development. Numerous industry and service companies, as well as public contracting authorities, constitute our client base. Furthermore, the institute cooperates with various academic and non-academic research institutes in developing innovative technologies.

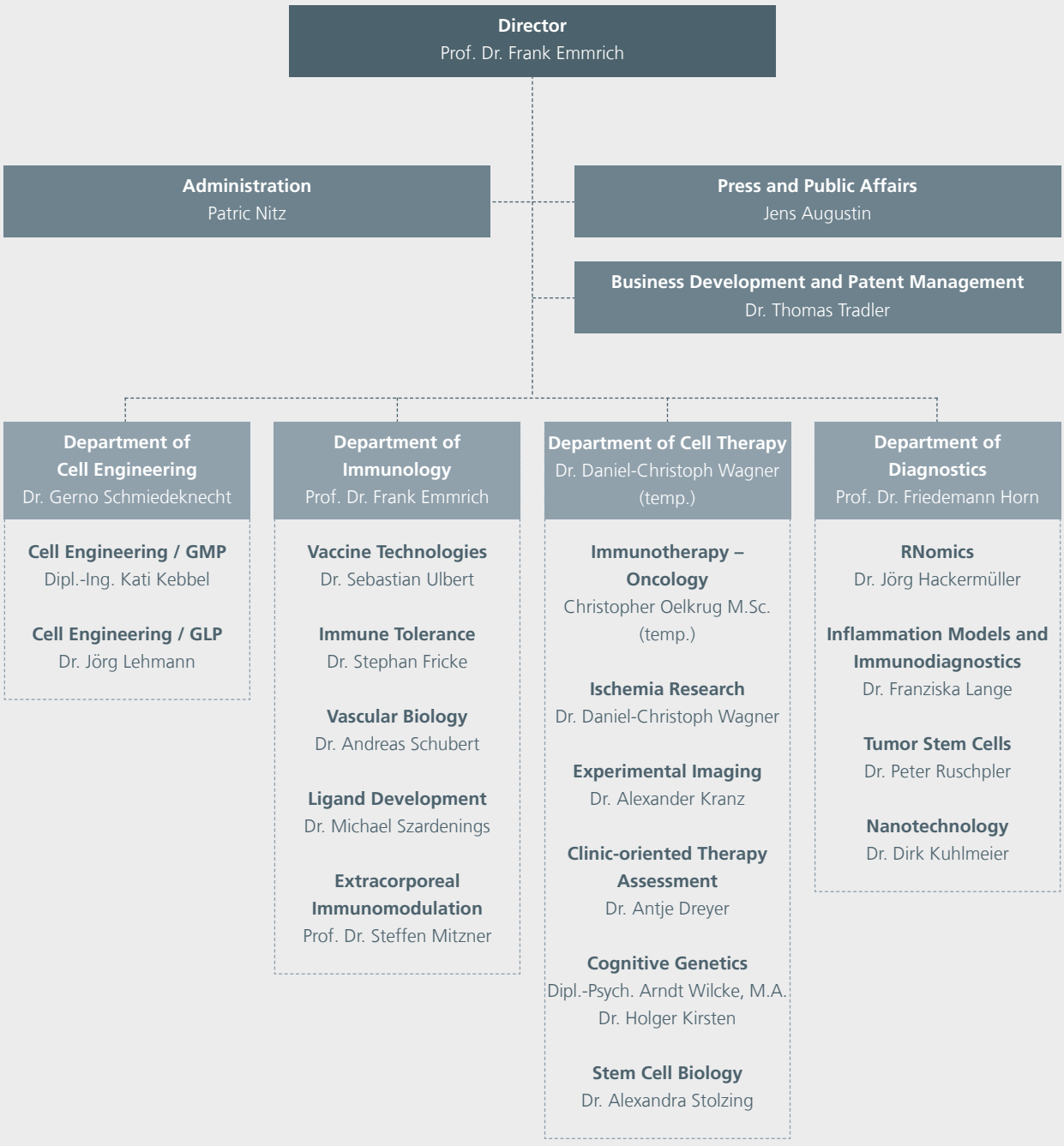
The institute is particularly proud of the ability to offer its clients a varied and wide range of services within the fields of drugs, cell therapy, diagnostics and biobanks. The executive department "Business Development / Patent Management" sees itself as a central point of reference in terms of communicating the most suitable services to clients and partners.

Press and Public Affairs

As an institution of applied research, the Fraunhofer IZI places great value on information provided by clients and the public. The executive department "Press and Public Affairs" coordinates the institute's internal and external communication. Through publicity events, the department assumes the institute's responsibility to inform and enlighten the public with respect to ongoing research. Furthermore, the executive department organises the annual "Fraunhofer Life Sciences Symposium" and the biannual "World Conference on Regenerative Medicine". Through both these events, the institute promotes scientific exchange and particularly helps to bring together the different research disciplines involved in regenerative medicine.

Administration

The lean and efficient administration of the Fraunhofer IZI is broken down into the departments IT, technology and business administration. Together with an external service provider, the IT department looks after the entire infrastructure. Through proficient in-house activities, cost-effective procurement of spare parts, and a series of energy-related optimizations within the areas of equipment and building technology, considerable savings were made with regards to operating costs. Through increased regulations and commercial processes within the areas of travel, procurement and personnel, the workload has increased in the business administration area. This challenge was addressed by further training and expansion of skills in order to make full use of employees' potential.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Inflammation Models and Immunodiagnostics
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Tumor Stem Cells
Dr. Peter Ruschpler
Nanotechnology
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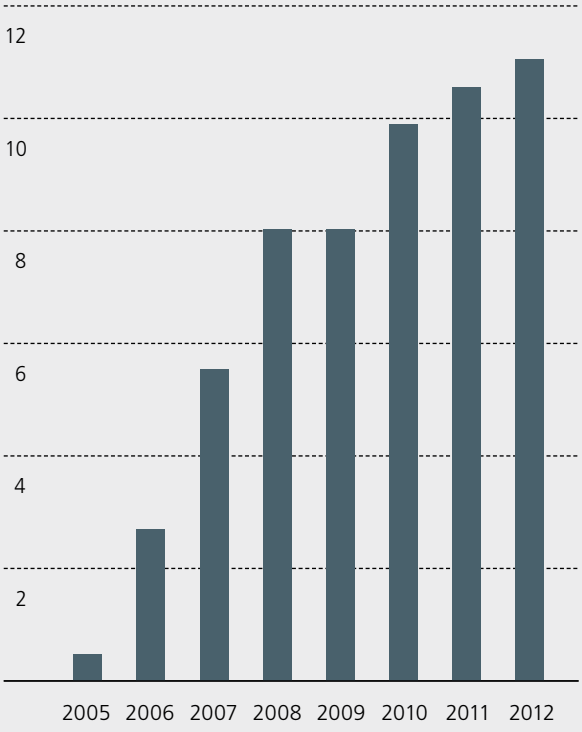
THE INSTITUTE IN NUMBERS

Financial volume

Mio €

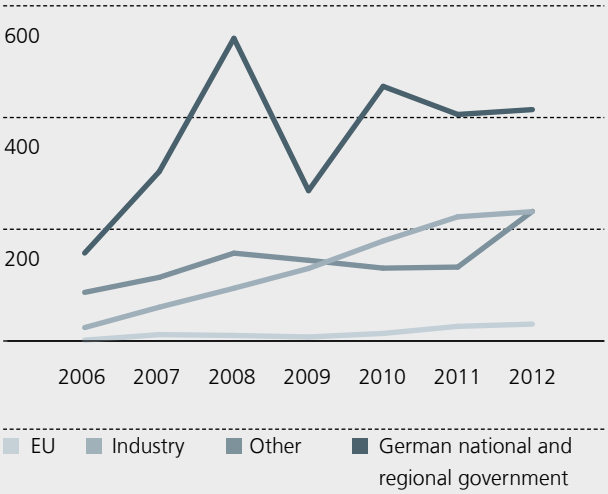


Overview of the projects

	number 2012	volume 2012
German national and regional government	18 (34%)	4 142 000 €
EU	2 (4%)	302 000 €
Industry projects	21 (40%)	2 315 000 €
Other (incl. internal programs)	12 (22%)	2 322 000 €
Total	**53**	**9 081 000 €**

Projects by volume

T Euro



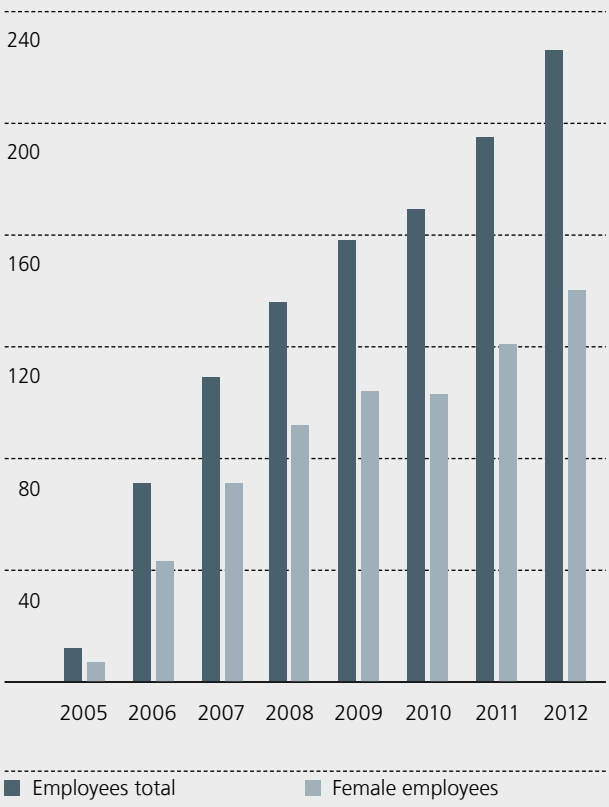
Budget

The institute's financial value increased to almost 11 million euros in the reporting year. The balance built up in 2011 was able to be retained and serves to hedge against financial uncertainties and the start-up costs arising from putting the first extension building into operation, as well as to finance the institute's own research projects and investments.

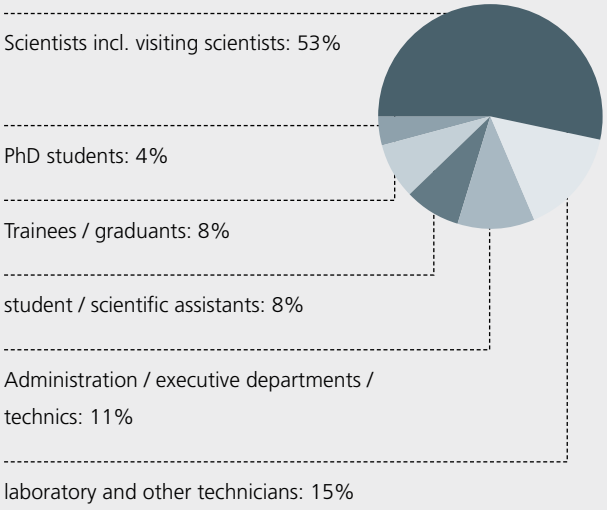
Projects

Project value was able to be increased to nearly 9 million euros in 2012. The successful acquisition of further large-scale projects led to another increase in average project value. 53 projects are being handled at present. As in the past, industry projects constitute the majority of our project work, accounting for 40 per cent of our overall volume, while publicly funded projects are of greatest financial value, worth over 4 million euros.

Employees

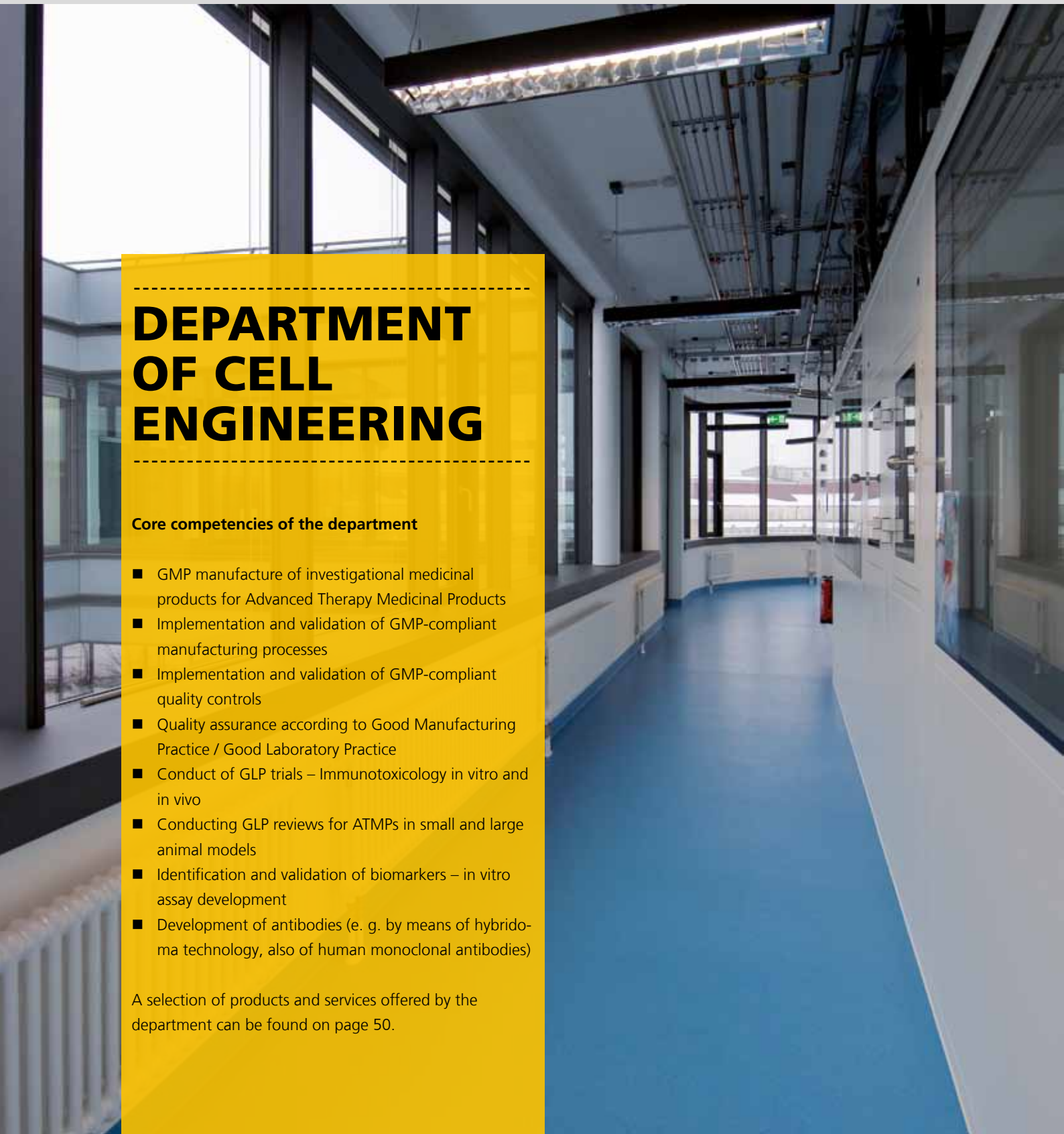


Workforce composition



Human resources

The number of employees at the Fraunhofer IZI attests to the trend observed in recent years and has risen by around 15 per cent. At the end of the year, the institute had 226 members of staff. This includes everyone who contributed to the institute's success, including guest researchers working at the institute. The growth in employee numbers is not exclusively concentrated on one particular group of employees, but is observed across the board. According to these numbers, the proportion of scientific and technical staff as well as staff working in the infrastructural areas has remained fairly constant compared with the previous year. At 62 per cent, the above-average proportion of female staff could also be maintained in 2012. One of the institute's major targets is to gain and retain excellent, junior research staff; in this respect, we place great emphasis on the supervision of up-and-coming scientists. In 2012, around 30 students, including PhD students, were supervised at the institute in drawing up their theses.



DEPARTMENT OF CELL ENGINEERING

Core competencies of the department

- GMP manufacture of investigational medicinal products for Advanced Therapy Medicinal Products
- Implementation and validation of GMP-compliant manufacturing processes
- Implementation and validation of GMP-compliant quality controls
- Quality assurance according to Good Manufacturing Practice / Good Laboratory Practice
- Conduct of GLP trials – Immunotoxicology in vitro and in vivo
- Conducting GLP reviews for ATMPs in small and large animal models
- Identification and validation of biomarkers – in vitro assay development
- Development of antibodies (e. g. by means of hybridoma technology, also of human monoclonal antibodies)

A selection of products and services offered by the department can be found on page 50.

IN CONVERSATION WITH DR. GERNO SCHMIEDEKNECHT

The reporting year saw the completion of the first extension building. What steps are now to be taken to put the new clean room facility into operation? The next steps involve integrating the new clean room facility into our existing quality assurance system and then qualifying all of the facilities and equipment in accordance with Annex 15 of the EU GMP guidelines. Qualification should be understood as the accurately documented evidence that facilities and equipment are suitable for the planned manufacturing activities. This is divided into the categories of design qualification, installation qualification, operational qualification and performance qualification. Even for a simple piece of equipment such as a refrigerator, this qualification is sometimes associated with file full of documents! As part of the integration of the new facilities into our quality assurance system, our fifty-plus general standard operating procedures (SOPs) have to be adjusted and expanded in such a way that they take into consideration both the existing and the new facilities. This presents a huge challenge and a great deal of work. Once this work has been completed, we aim to obtain initial manufacturing authorization in accordance with Section 13 of the German Drug Act (AMG) for the new clean rooms, which also entails an official inspection. For this to happen, it is likely that one of the existing manufacturing projects from the established facility will initially be expanded in order to achieve an increased throughput of investigational medicinal products.

For several years now, two large-scale projects focusing on the development of new cancer therapies have been handled within the department together with international industry partners. What successes were able to be achieved in this area in the 2012 reporting year? In 2012, we were able to move both projects forward to a stage which, from a regulatory, substantial and logical perspective, will enable the clinical trials planned by our project partners to commence in 2013. This was achieved by implementing certain measures, for example obtaining the necessary manufacturing authorization in accordance with Section 13 AMG and various import licenses in accordance with Section 72 AMG, training new members of staff, and qualifying new external premises for storage and packaging in BIO CITY Leipzig, which were then integrated into our manufacturing authorization. Furthermore, the manufacturing and testing documentation was optimized and harmonized in line with the project partners' other manufacturing sites involved around the world. Comparability studies were carried out with the project partners' other manufacturing sites and the validation of analytical methods was driven forward. As far as I can see, there should be nothing else standing in the way of the clinical trials!

Which new projects were initiated in the department in 2012? In the Cell Engineering / GLP Unit, a large cooperation project with Nuvo Research GmbH got under way, which is funded by the Sächsische Aufbaubank (Saxon Development Bank, SAB). This project involves preclinical tests to determine the efficacy of an important active ingredient developed by the project partner using a specialized animal model developed by the unit. The Cell Engineering / GMP Unit's existing clean room facility was working to full capacity in 2012, which meant that there was unfortunately no infrastructure available to take on new projects. The unit therefore focused on conducting existing projects. The extension work carried out in 2012 has created additional capacities for new projects. By and large, with regard to highly regulated areas such as GMP and GLP, the quality of projects is always placed ahead of the quantity. Only by putting quality first can we meet the strict legal requirements and fulfill our customers' high demands.

Applied research aims to translate findings into clinical practice. How is this process structured in the Department of Cell Engineering? In the Department of Cell Engineering, innovative processes, procedures and tests generated through research and development have to be adapted to the strict legal guidelines (such as GMP, GLP, etc.) in such a way that a safe application is possible during subsequent preclinical and clinical trials. This is achieved at the institute by obtaining manufacturing authorizations in accordance with Section 13 of the German Drug Act (AMG), tissue procurement authorizations in accordance with Section 20b, or GLP certificates, which partly represents at least an entire year's work for one single project.

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UNITS

Cell Engineering / GLP Unit

The unit focuses on three main topics: 1) Planning and conduct of efficacy and safety studies (biodistribution, tumorigenicity, immunotoxicity, immunogenicity) in the context of the approval of new pharmaceuticals, medical devices and chemicals under GLP conditions (in vitro and in vivo). This also includes the development, establishment and validation of new in vitro and in vivo models. 2) Identification and validation of new protein biomarkers for the diagnosis and therapy of chronic-inflammatory diseases, tumor diseases and for the sector of veterinary medicine / animal breeding. 3) Development and optimization of methods and techniques for the diagnostic detection of protein biomarkers and for the separation of cells. This includes the development, manufacture, and modification of monoclonal antibodies as well as the participation in the development of analytical instruments and cell separation robots.

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Cell Engineering / GMP Unit

This unit operates a state-of-the-art clean room facility for the provision of investigational medicinal products according to Good Manufacturing Practice (GMP). Their expertise is in the field of Advanced Therapy Medicinal Products (e. g. tissue engineering products, somatic cell therapeutics). Here, the whole range from process development and validation to the manufacture of investigational medicinal products is covered.

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PROJECTS

Development and usage of new on-farm procedures for examining performance in terms of health stability and fertility in German Holstein cows

The main goal of this interdisciplinary joint project is to develop new, innovative procedures to examine the performance of dairy cows of the German Holstein breed in terms of fertility and health traits, which is to be recorded directly at the breeding farms (on-farm recording). This involves recording key traits which will then be used to establish appropriate breeding procedures. Sub-project aims are the investigation and breeding-related usage of parameters of fat mobilization dynamics, of female fertility, and traits pertaining to the stability of health. These will be based on a semi-automated, infrared-image analysis for the indication of inflammation on extremities and the udder as well as a semi-automated determination of immunological parameters in milk.

The Fraunhofer IZI is attending to the selection and validation of known immunological biomarkers for the health stability of highly productive dairy cows. New, potential biomarkers are also to be identified. Three medical condition clusters have been defined for this purpose: 1) mastitis, 2) systematic diseases (e. g. endometritis) and 3) mastitis plus a systematic disease. Potential biomarkers have been identified in cells from milk samples in these clusters and, for comparison, in healthy animals by means of DNA microarray and real-time PCR on an mRNA level. Besides this, several potential biomarkers were also directly verified as soluble protein in the milk by means of ELISA, as long as test kits were available for the respective markers. Promising candidates were validated by means of random sampling in 100 animals from different farms. Following validation, three candidates were confirmed as biomarkers for one or several of the three disease clusters.

In a further stage of the project, monoclonal antibodies against these proteins will be developed until April 2013, which will assist in developing laboratory tests. These laboratory tests will be used later in the field validation of the biomarkers on three selected farms.

As part of a follow-on project, it is to be determined to what extent the discovered biomarkers may also be of laboratory diagnostic value for veterinary medicine.

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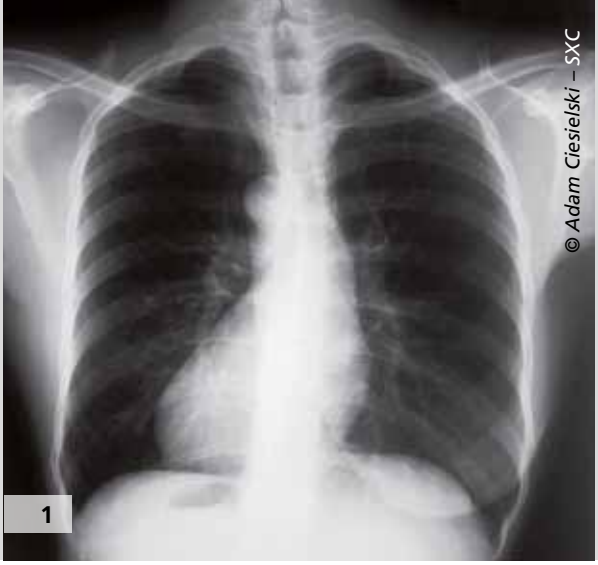

Ultrasensitive detection of protein biomarkers in exhaled breath condensate for the non-invasive, early diagnosis of bronchial carcinoma

Numerous proteins can be detected in exhaled breath condensate and used diagnostically, including cytokines and angiogenic mediators. In preliminary work it was demonstrated that VEGF (vascular endothelial growth factor) is more prominent in lung diseases, however the concentrations in pleural effusion are not absolutely conclusive in terms of selectivity. However, initial investigations into exhaled breath condensate have shown that an excellent degree of separation is possible in bronchial carcinoma patients who have not yet started treatment.

The primary objective of the project is to detect VEGF as a biomarker for the early diagnosis of bronchial carcinoma using an innovative device system.

VEGF may have been identified as a promising biomarker candidate in preliminary work, however investigations have not yet been conducted to find out to what extent this biomarker permits a sufficiently early recognition of lung cancer in routine use and can thus significantly improve individual chances of recovery. The methods used so far are not suitable for routine use.

The joint partners Fraunhofer IZI, the Institute for Clinical Immunology at the Medical Faculty of the University of Leipzig, Compart Umwelttechnik GmbH based in Weissenfels, and GESA Automation GmbH based in Teuchern are developing a completely new device platform which integrates the acquisition of breath condensate and the diagnostic detection of VEGF in breath condensate. This system can be used to conduct a clinical diagnostic trial as a follow-up to the project. By adapting the sampling modules of the device platform at a later stage, these protein biomarkers could also be detected in sample materials other than in exhaled breath condensate, such as in body fluids (e. g. plasma, urine, cerebrospinal fluid) or in cell or tissue lysates from biopsy samples. The system could be developed further to also detect biomarkers for the early diagnosis of other tumor, autoimmune or degenerative diseases. Whilst, at present, only specialized laboratories are generally able to detect such biomarkers, making application logistically complex and very expensive, the international trend is clearly heading towards point-of-care diagnostics, i. e. the quick and easy detection of such biomarkers directly at doctor´s office. This, in turn, poses an enormous challenge for the developers of such device systems. This is the challenge we have set ourselves in this project. The project will be successfully completed in January 2013 when the prototype is presented. Plans are in place to expand the technology to other applications as part of a larger joint project.

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1 *Imaging procedures such as chest X-rays do not detect bronchial carcinoma until a relatively late stage. Earlier diagnosis would improve the chances of finding a cure.*

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2

Process transfer and manufacture of the immunotherapeutic DCVax® L-Drug

The American biotechnology company Northwest Biotherapeutics Inc. is planning to conduct a phase III placebo-controlled clinical trial to examine the efficacy of their immunotherapeutic DCVax®-L. DCVax®-L is an advanced therapy medicinal product (ATMP) based on autologous dendritic cells to treat glioblastomas, a particularly aggressive type of brain tumor. The therapeutic agent already has been and is being successfully used in clinical trials in the USA. As part of the project, the existing GMP manufacturing process, including quality controls, was transferred to Leipzig by the American manufacturing company Cognate BioServices Inc., where it was also adapted to the European legal foundations which are stricter in some respects. Once all of the documents have been issued (i. e. manufacturing formula / instructions / protocols, product specifications, test instructions / protocols, specifications), the next stage focusses on the manufacturing and quality control of several test batches in order to structure the manufacturing process and quality controls in the Fraunhofer IZI's clean rooms and quality control laboratories. The next step was process validation, which included the fully documented manufacturing and quality control of three validation batches. Besides process validation, the validation of analytical methods to detect identity, purity, efficacy and safety has begun and / or already been carried out. Above all, this includes the validation of: Flow cytometry, the regulation of in vitro efficacy by means of the COSTIM bioassay, testing bacterial endotoxins, and examining sterility. Very complex methods such as flow cytometry and COSTIM bioassay will continue to be validated in 2013. Furthermore, it was necessary that leukapheresis procurement facilities and neurosurgical tumor procurement centres were qualified to guarantee high-quality procurement and testing of patients' autologous base materials. The required authorization for tissue procurement in accordance with Section 20b (2) of the German Drug Act for the procurement of tumors presents a particular challenge here. A manufacturing authorization specifically for DCVax®-L and DCVax® placebo was issued in July 2012 in accordance with Section 13 of the German Drug Act as a result of this complex work, following a two-day acceptance inspection by the responsible pharmaceutical supervisory authorities (Landesdirektion Sachsen and the higher federal authority Paul-Ehrlich-Institut). Once this manufacturing permit had been obtained and additional necessary preliminary work carried out (e. g. the authorization application for the clinical trials by the sponsor Northwest Biotherapeutics, development / validation of additional quality controls and / or improvement of existing quality controls), the focus in 2013 should move to the manufacture, quality control and provision of the clinical investigational products for Germany and the UK.

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1 / 2 *Manufacturing DCVax® L-Drug (Brain) in the clean room facility at the Fraunhofer IZI.*

DEPARTMENT OF IMMUNOLOGY

Core competencies of the department

- Vaccine development
- Tolerance induction
- Antibody development
- Immunological models
- Phage display of peptides and antibodies
- Rheologic models
- Antimicrobial peptides
- Cellular adsorbers

A selection of products and services offered by the department can be found on page 50.

IN CONVERSATION WITH PROF. DR. FRANK EMMRICH

Fraunhofer IZI researchers are also involved in a project group in Rostock. What is the topic and how is this collaboration work panning out? The group in Rostock is primarily dealing with extracorporeal immunomodulation, which means it is developing technologies with which cells from the human immune system will be treated outside of the body and then passed back in a continuous flow. A core topic here is the treatment of sepsis – a condition whereby the organism is severely damaged by germs and an out-of-control immune response. The therapeutic application of antibiotics does not remove the large amounts of germs which have been killed, yet are still bioactive. Using the extra-corporeal therapeutic approach, the patient's blood is taken, cleansed of germs and other harmful substances using biological and mechanical procedures right beside the hospital bed, and then fed back to the patient. Initial clinical trials in the field have already been completed and demonstrate great potential in this development. Similar methods are also being established in the area of dialysis technology. An additional core topic concerns the development of model systems for the human intestinal wall which can be used to test active agents, for example. Following the initial start-up phase, the project group has now fully commenced with its activities. As there are numerous links with the units in Leipzig, we hope that strong synergies can be formed here.

The department has been coordinating a large EU project since 2011. Which experiences and successes were able to be gained as part of this project in the meantime? The EU project WINGS brings together academic and industry partners from Europe and the USA, and is concerned with developing technology for the diagnosis and prevention of West Nile Virus (WNV) infections. This makes it highly topical as this virus, which is transmitted by mosquitos, is continuing to spread across Europe. Italy and Greece in particular, but also a number of other southern European countries, again experienced hundreds of infections in 2012, many of which ran a severe, neurological course and some of which were even fatal. Until now, such high numbers of cases were only really known in the USA, where WNV appeared in 1999. The number of WNV cases in the USA also reached its peak in 2012. So far, the collaboration project has seen many milestone successes. For example, the first vaccine candidates have been developed and are currently involved in preclinical testing. The focus here is largely on types of technology which can be used to vaccinate older people or people with a weakened immune system, as these target groups are particularly vulnerable to WNV. These results are very promising and we are confident that we will be able to deliver respective vaccines for tests on human subjects at the end of the project in 2014. Keeping in contact with our partners in the WNV-endemic countries is also important for the development of vaccines and specific diagnostic agents. Maintaining this contact ensures that technical developments can constantly be adjusted to the viral strains circulating at the time. This is essential in the case of WNV, which can modify its genome very quickly.

Which new projects were taken on in 2012 and what are the department's future plans? Last year we were able to vastly expand our competencies, establish new collaborations and consolidate existing partnerships in projects. In developing innovative vaccines, important research contracts were secured from within the vaccine industry. Improved gene libraries are being developed in the area of peptide diagnostics and active agents, which are now also being applied in a large Fraunhofer-Gesellschaft collaboration project in the identification of the molecular structures of allergens, their detection and methods of removing them in the food industry. This project will be handled in both the Department of Immunology and the Department of Cell Engineering as of 2013. Furthermore, we have made key progress in the preclinical development of methods to fight transplant rejection. Last but not least, the findings with plant compounds in fighting tumors led to the spin-off company Oncotrition GmbH being established in Leipzig, which will drive forward the development of these therapeutic approaches to clinical application in close collaboration with the Department of Immunology and the Department of Cell Therapy.

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UNITS

Vaccine Technologies Unit

The unit is developing vaccines for a variety of infectious diseases in the field of human and veterinary medicine, as well as diagnostic test systems. Primary activities include research into recombinant protein and DNA vaccines for viral zoonotic infections. In addition, novel ways of inactivating microbes for use in vaccines are being developed.

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Immune Tolerance Unit

The unit develops cell- and antibody-based therapeutic strategies to treat complications following hematopoietic stem cell transplantation. Novel concepts of immunological tolerance oriented towards immunologic and therapy associated complications (e. g. GVHD) are being tested in new, in-house developed animal models.

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Ligand Development Unit

The unit is developing peptide ligands with special phage display libraries, besides exploring technologies for the practical application of the ligands. Our work is focused on mapping binding sites of defined antibodies and also antibody mixtures from individual patient sera (e. g. in the case of allergy or infection), individual immune response, and identifying novel targets on cell surfaces and binding sites on therapeutically or diagnostically relevant proteins. Our goals are to modulate the immune system and develop potential peptide therapeutics, as well as to develop diagnostics and affinity purification media.

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Vascular Biology Unit

The unit develops new therapies for the treatment of atherosclerosis. Using shear stress models, genes and promoters are identified that can be activated by biomechanical forces. Another focus of the unit is the establishment of a therapy against oral streptococcus species. Furthermore, antimicrobial peptides are being developed and tested for the food industry and for medical applications.

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Extracorporeal Immunomodulation Unit

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

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PROJECTS

Specific diagnosis of infections with the West Nile Virus

The West Nile Virus (WNV) is continuing to spread across Europe and is already viewed in some countries, such as Greece or Italy, as endemic. The virus leads to flu-like symptoms in approximately every fifth infected person, but can also cause severe, neurological complications such as encephalitis or meningitis, which can be fatal. In order to be able to compile verified data on the spread of WNV, ways of specifically detecting an infection are essential. A direct detection of the virus, e. g. in the blood, is however only rarely possible as WNV has usually already disappeared from the bloodstream once the disease's symptoms emerge. This is why indirect detection methods are usually drawn on, for example by searching for antibodies formed against WNV. This type of diagnostics, however, is complicated by a pronounced cross-reactivity of antibodies: WNV belongs to the family of flaviviruses which also includes the pathogens for yellow fever, tick borne encephalitis or dengue fever. As these viruses are all extremely similar in terms of their structure, respective antibodies are able to disrupt current tests, above all in regions where different types of flavivirus are found at the same time. Every positive result therefore has to be confirmed using elaborate and expensive virological tests.

The Fraunhofer IZI Vaccine Technologies Unit is coordinating the EU project WINGS ("Epidemiology, Diagnosis and Prevention of West Nile Virus in Europe") which involves the development of technologies for the specific diagnosis of infections with WNV. For this project, the virus was dissected into small fragments which constitute individual epitopes for antibodies. Sera from individuals living in endemic areas who are infected with WNV or other flaviviruses are now being used to identify epitopes which are specific for anti-WNV antibodies. Several candidates of this type could already be identified and are now in the process of being further developed for diagnostic testing,

Using this technology established at the Fraunhofer IZI, valuable findings could also already be gained on the humoral immune response to WNV. The system can also easily be adapted to genetic modifications of the virus. This is particularly interesting when bearing in mind that WNV is a global problem and that more and more mutations of the virus are emerging which, in some respects, differ considerably from each other in terms of their virulence – the ability to trigger severe infections. Finding out how the human immune system reacts to WNV is extremely helpful here for the development of vaccines and treatments.

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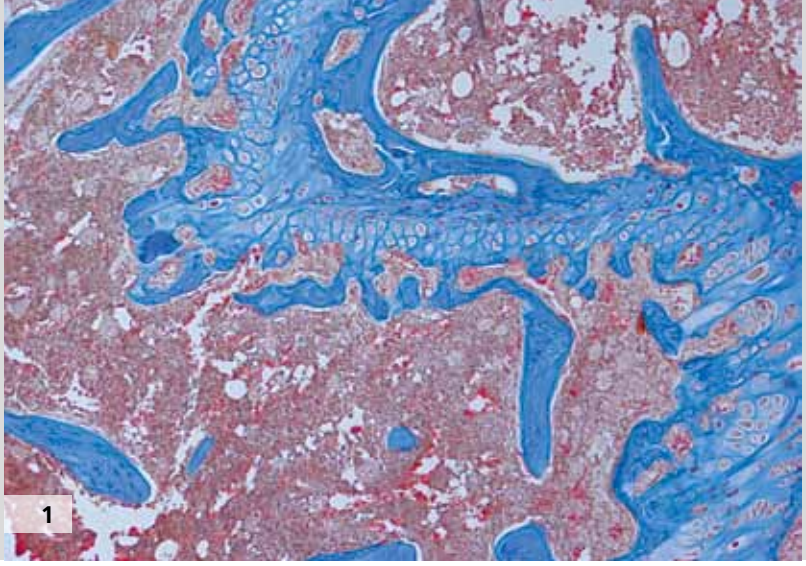
SEVENTH FRAMEWORK PROGRAMME

West Nile Shield Project
WINGS



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The influence of tolerance-inducing anti-human CD4 antibodies on the graft-versus-tumor effect (GvT) following allogeneic hematopoietic stem cell transplantation

The main complication following allogeneic hematopoietic stem cell transplantation is acute graft-versus-host-disease (aGvHD). Besides conventional immunosuppresive agents, OKT3-antibodies, interleukin-2 receptor antibodies or anti-thymocyte globulin to name just a few are also being used to treat this disease, though they are often associated with low-level long-term success and toxic side effects. In addition, these types of therapy suppress the entire immune system and with this also the immunologically significant anti-tumor effect of the immune cells (graft-versus-leukemia effect). This GvL effect must however be maintained in order to prevent the risk of the underlying disease (leukemia) returning in the patient.

Due to the need for innovative and less stressful forms of therapy, murine GvHD and leukemia transplantation models were developed within the unit. These models were able to be used, among other things, to establish human immune systems in mice. In due consideration of the GvL effect, these models enable the testing of active agents for the prevention and treatment of GvHD, which would be immediately conceivable for clinical application on human subjects. The focus is on the investigation of the influence of various anti-human CD4 antibodies on the GvHD with due regard to the GvL effect. So far, it could be demonstrated, for example, that the emergence of aGvHD following allogeneic hematopoietic stem cell transplantation could be prevented in the long term through the ex vivo incubation of a transplant with the anti-human CD4 antibody MAX.16H5. This involved the use of a mouse model which also displays features of the human immune system.

A GvHD-NOD/SCID mouse model and a leukemia mouse model will be further developed at a later stage in the project. Furthermore, anti-CD4 antibodies will be introduced in the treatment and prevention of GvHD as therapeutic agents until clinical application is possible. New findings from antibody therapy for the transplantation of solid organs and for other immunological disease patterns (e. g. autoimmune diseases) will also be deduced. Besides a new type of antibody therapy, insights into immunological processes of GvHD and the GvL effect are to be expected. These insights may be extremely valuable not just for hematopoietic stem cell transplantation, but also for the transplantation of solid organs and for application in other indications (e. g. autoimmune diseases).

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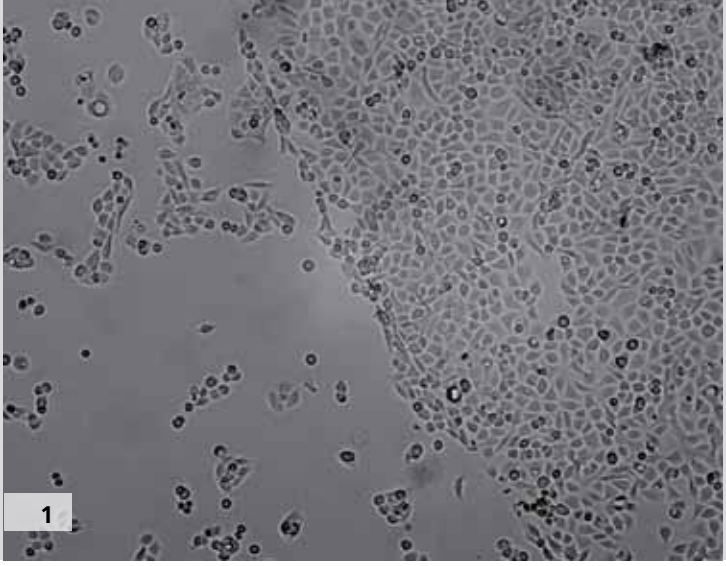
1 *Reconstituted bone marrow of recipient mice treated with antibodies following allogenic stem cell transplantation.*



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Novel peptide technologies

Modern phage display technologies at IZI enable the use of peptide libraries in the scale of 10^{10} sequences and beyond; by applying in vitro recombination, for example, more than 10^{15} sequences are accessible. Not only does this allow standard applications to be handled; it also permits completely new tasks to be approached. We are currently cooperating with a German company to produce even more complex libraries based on a novel DNA synthesis method, which allows the amino acid distribution in the library to be controlled. Epitope mapping of monoclonal antibodies is a routine activity, which enables the identification of binding peptide sequences. This does not only give detailed information about the binding site of the antibody but is also useful, for example, in comparing clones of monoclonal antibodies. The identified sequences are identical to the antigenic region of protein sequences, or they can be alternatively allocated using special software. Many of such projects were completed in 2012. By making a direct comparison between mapping with synthetic peptides and Ala scan mapping of epitopes, we were able to show that the results from our libraries with multiple identified binding sequences give comparable results. This enables the identification of all relevant amino acids within the epitope. The complexity of our libraries also allows us to map complex antibody mixtures. Together with the Helmholtz Centre for Environmental Research in Leipzig, we identified a large number of peptides that are similar or identical to known allergens. For some of these peptides we have now been able to isolate the corresponding antibodies from patient sera. For this and also other applications, antibodies are usually viewed as state-of-the-art tools. In order to be able to use peptides in these areas, we are looking for novel methods and simple procedures. In an early project conducted together with the Fraunhofer IFAM, we discovered that a simple enzyme reaction can be used to bind peptide ligands covalently to their cell surface receptors. This resulted in the institutes coming together to start the ZELLFIX project, which is funded by the Fraunhofer-Gesellschaft, in order to apply the same reaction to modify surfaces. Cells often do not attach well to the polymer surfaces of culture dishes. Polystyrene surfaces are usually treated with plasma, which can result in an uncontrolled production of compounds which are often toxic. Using our new approach could immobilize peptide and protein ligands, thus improving the adhesion of cells as well as directly achieving the covalent coupling of cell surface proteins, as is the case with plasma activated surfaces. The ZELLFIX project has confirmed our original assumptions. Even small, defined areas of cell culture dishes can be modified to allow the attachment of cells only in specific areas. The method is also suitable for improving the binding of proteins to commercially available surfaces which have already been plasma activated. These procedures are already being tested with partners from the industry and the Fraunhofer-Gesellschaft for initial special applications. Meanwhile we have made completely new discoveries regarding enzymatic reactions, which will facilitate applications beyond biological and medical application areas.

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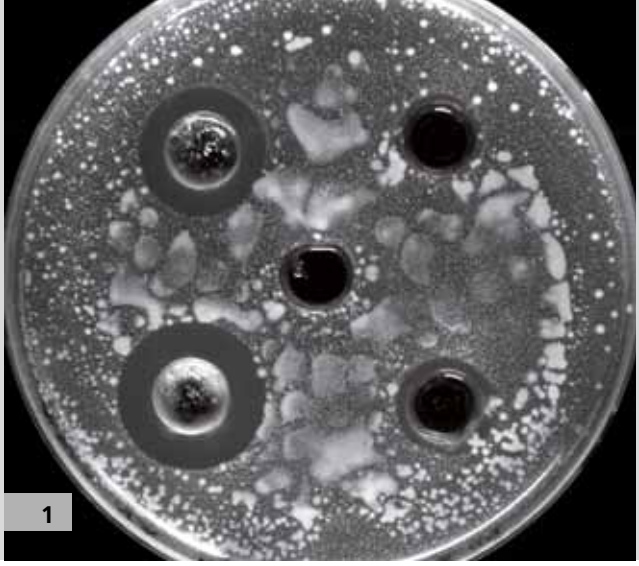
1 *"To stick or not to stick": A simple form of enzymatic treatment transforms a normal Petri dish into a cell culture dish (surface in right section of the image).*



Development of therapeutically effective peptides for the treatment of contagious and tumor diseases

The need for new, effective drugs based on bioactive substances has increased greatly in recent years. The predictions for the future also reveal strong growth in this segment. This trend was picked up on in the Vascular Biology Unit and a technology platform was created which is able to develop and evaluate peptides both against multi-resistant hospital germs and also against tumor cells. This DNA-based technology allows an appropriate, antibiotically effective peptide to be developed against every relevant hospital germ by means of a high-throughput technique. Some of these antimicrobial peptides have a broad-spectrum effect and could thus be applied against a number of different types of bacteria or also pathogenic fungi (e. g. candida albicans).

During the course of 2012, several sequence libraries were established with partly differing ranges of efficacy, e. g. against human-pathogenic oral germs (cariogenic germs such as streptococcus mutans, streptococcus sobrinus or pathogens associated with paradontitis such as actinobacillus actinomycetemcomitans, porphyromonas gingivalis), germs found in the gastrointestinal tract (heliobacter pylori) and also against germs found in the respiratory tract (haemophilus influenzae).

The use of bioactive substances from plants, insects and amphibians for the treatment of inflammations and also tumor diseases (e. g. the so-called "frog vaccine") has been common practice for a number of years, particularly among the indigenous peoples of Central and South America. This is why, together with the Immunotherapy – Oncology Unit, peptides from the skin secretion of tropical frog species (e. g. phyllomedusa bicolor) were cloned in an additional experimental approach and several amino acids from these peptides were mutated at defined positions. Compared with the original peptides, it could be demonstrated in vitro that the cytotoxicity of these peptides, in comparison with tumor cells, could be increased by modifying the amino acid sequence, while control cells showed a comparably high level of resistance. Although the mechanism of action of these peptides was not yet able to be clarified, the assumption suggests that the different composition and net charge of the cell membrane of tumor cells and non-tumor cells play a decisive role here. Moreover, some of these peptides may have an additional, immunomodulatory effect.

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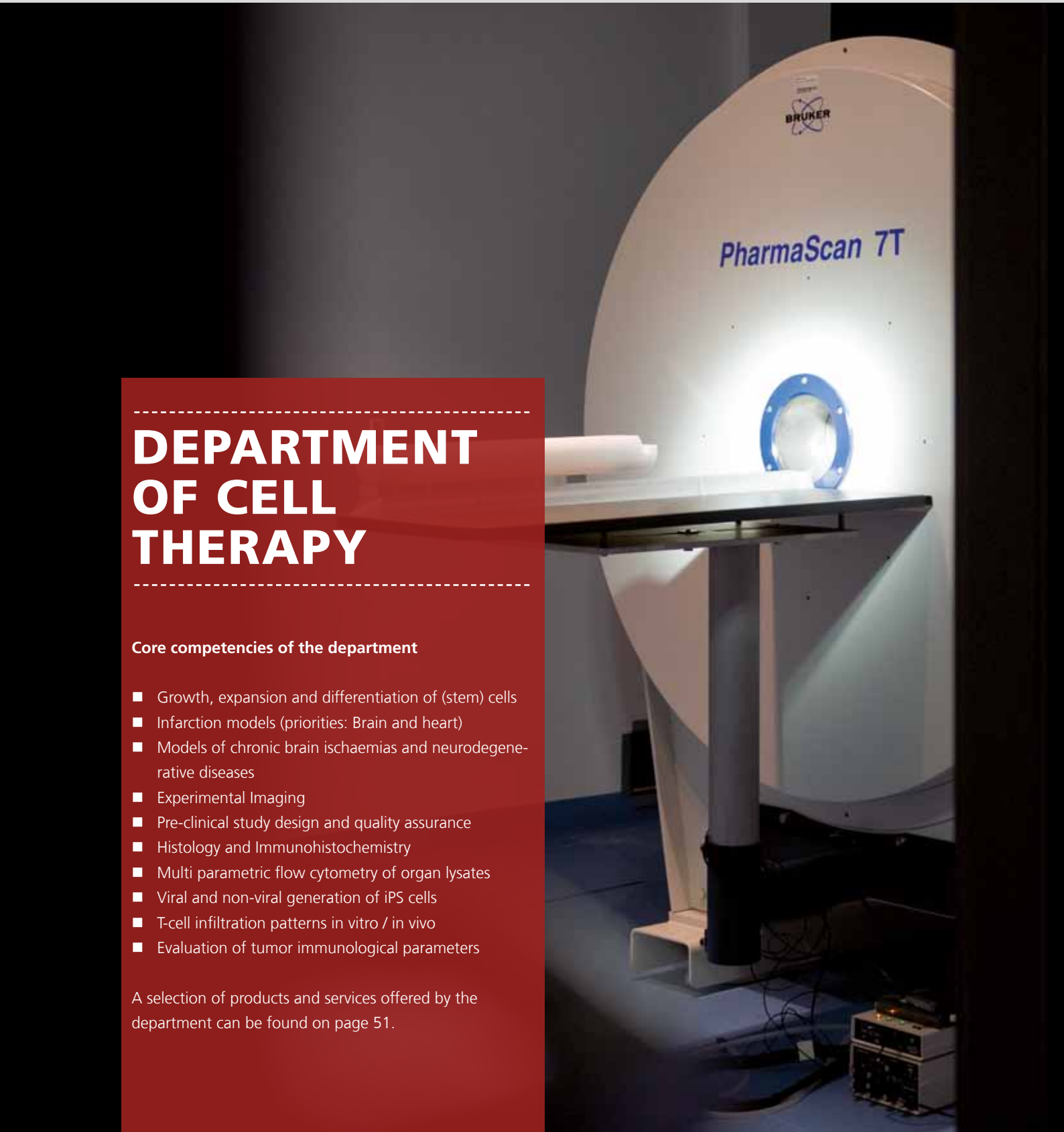
1 *Agar diffusion method on coliform germs with modified antimicrobial peptides (top left sequence 1, top right sequence 2, bottom left sequence 3, bottom right sequence 4, centre unmodified output sequence).*

2 *Agardiffusionstest an Candida spec. mit einigen modifizierten antimikrobiellen Peptiden (links oben Sequenz 1, rechts oben Sequenz 2, links unten Sequenz 3, rechts unten Sequenz 4, Mitte unmodifizierte Ausgangssequenz).*



DEPARTMENT OF CELL THERAPY

Core competencies of the department

- Growth, expansion and differentiation of (stem) cells
- Infarction models (priorities: Brain and heart)
- Models of chronic brain ischaemias and neurodegenerative diseases
- Experimental Imaging
- Pre-clinical study design and quality assurance
- Histology and Immunohistochemistry
- Multi parametric flow cytometry of organ lysates
- Viral and non-viral generation of iPS cells
- T-cell infiltration patterns in vitro / in vivo
- Evaluation of tumor immunological parameters

A selection of products and services offered by the department can be found on page 51.

IN CONVERSATION WITH DR. DANIEL-CHRISTOPH WAGNER

The Neuro / Cardiorepair Unit was restructured in 2012. What consequences have arisen from this with regard to the orientation of the department? The unit was restructured for both organizational and also research and content-related reasons. Due to the high project volume and the associated rise in staff numbers, all research projects involving large animal models were organized and brought together in the new Clinic-oriented Therapy Assessment Unit. The aim of the Experimental Imaging Unit – also a new addition – is to pool and synergistically apply the increasingly available and sophisticated imaging technologies. The key areas of stroke and heart attack are now investigated more substantially under the heading of ischemia. Particular attention is given not only to the inflammation and autoimmune processes, which follow a similar pattern after an ischemic event, but also to chronic ischemias caused by microangiopathies. The strategic orientation of the department and the unit has therefore barely changed – we have merely deepened the focal points of our research and accommodated the increasing diversification. The new structure also allows us to react more specifically to requests in the different areas.

For many colleagues in the department, the completion of the first extension also marked the move into the new building. How have members of staff settled in and what advantages have arisen from the new facilities being put into operation? Moving the department presented a huge organizational and logistical hurdle which we have, fortunately, now overcome. The physical proximity of office, laboratory and functional spaces in the first extension building, which we were able to hugely contribute towards in terms of the building's design, signifies a considerable simplification of our workflows. The move into our own, long awaited facilities also marks the end of our almost seven-year status as guests at the University of Leipzig. Although we have experienced a great deal of support at the university, we were very much restricted in terms of space, especially in the laboratories, which also had an influence on the advancement of projects. Thanks to excellent working conditions in the extension building, we expect to be able to considerably increase our productivity. We are also extremely happy that we are now much closer to our colleagues in the main Fraunhofer IZI building; before the move, we mainly communicated with these colleagues via email.

In May, the department organized the "7th International Symposium on Neuroprotection and Neurorepair". How would you personally sum up the event? Many members of the department have known and appreciated the ISN&N Symposium for years as participants; we therefore welcomed the opportunity to organize the meeting together with the founders from Magdeburg. A distinctive feature of the ISN&N is the joint participation of young up-and-coming researchers and selected, internationally successful colleagues, as well as the thoughtful selection of the conference location. This year's symposium in Potsdam has continued this tradition and was – in my opinion – shaped by excellent scientific talks and discussions, as well as an extremely animated and communicative atmosphere. With 330 attendees, it was also the largest event of the symposium series to date, since being established in 1998.

This year, the Nobel Prize for Medicine and Physiology was awarded to S. Yamanaka and J. Gurdon for the development of iPS technology. How does this recognition spur on the work undertaken by the Stem Cell Biology Unit, which uses an advanced version of the awarded technology? The Nobel Prize for the reprogramming of mature somatic cells to pluripotent stem cells has of course brought a great amount of public recognition to this branch of research that goes beyond the usual specialist literature. This could have a favorable impact on the interests of industry partners and public sponsors in the area and thus facilitate and accelerate the work of Dr. Stolzing (Head of the Stem Cell Biology Unit) and her colleagues. This would be important as many essential aspects of iPS technology still remain unresolved. Above all, this includes determining the most effective way of reprogramming, besides conducting investigations into the possible genetic and epigenetic abnormality of iPS.

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UNITS

Experimental Imaging Unit

Experimental imaging stands at the interface between engineering and life sciences. It supports research activities which require the acquisition and processing of imaging and involves various technical devices and software. Due to constantly evolving methods in magnetic resonance imaging, fluorescence, and bioluminescence technology the unit is constantly adapting its field of work to the latest developments. The main function is to apply current imaging methods to the tasks required by project partners.

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Immunotherapy – Oncology Unit

The unit encompasses two major interest areas. First our focus is directed at the development and testing of novel therapeutic strategies with the aid of innovative tumor models for the treatment of cancer patients. An additional focus centers on the enhancement of therapeutic cancer vaccines through different administration strategies, in view of the fact that tumor immunology and re-engineering of the immune system have shown promising results in contrast to current curative treatments.

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Ischemia Research Unit

The focus of this unit is the investigation and development of novel therapeutics and diagnostics for ischemic stroke and myocardial infarction. Preclinical evaluations occur stepwise from cell culture to animal models. The implementation of strict quality standards increases the predictive value of preclinical research and may therefore improve the translation of promising therapies to the clinic.

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Clinic-oriented Therapy Assessment Unit

The unit tests and develops innovative diagnosis and therapy procedures for stroke. As the possibility of being able to transfer findings from current laboratory small animal models to human patients is sometimes only very limited, a globally unique large-animal model was established for the translational approach. Using this model means that a therapeutic or diagnostic principle can be tested under conditions which come close to patient treatment in a clinical setting. Both the gyrencephalic brain structure and the size of the brain much more closely resemble the human situation in the sheep model as opposed to in the small animal.

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Cognitive Genetics Unit

The Cognitive Genetics Unit investigates the basic and applied genetics of cognitive processes. The focus of our work is on the genetics of dyslexia. Our main aim is to develop an early screening test to allow the functional regeneration of dyslexia-related cellular neurological deficits.

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Stem Cell Biology Unit

The unit combines insights from stem cell biology and biogerontology to develop novel strategies in regenerative medicine. We pursue different innovations to "rejuvenate" adult stem cells in vitro and in vivo, so that these cells can resume their function as promoters of regeneration, particularly in elderly patients. These cells are then used in an Alzheimer mouse model to verify the therapeutic potential of these cells.

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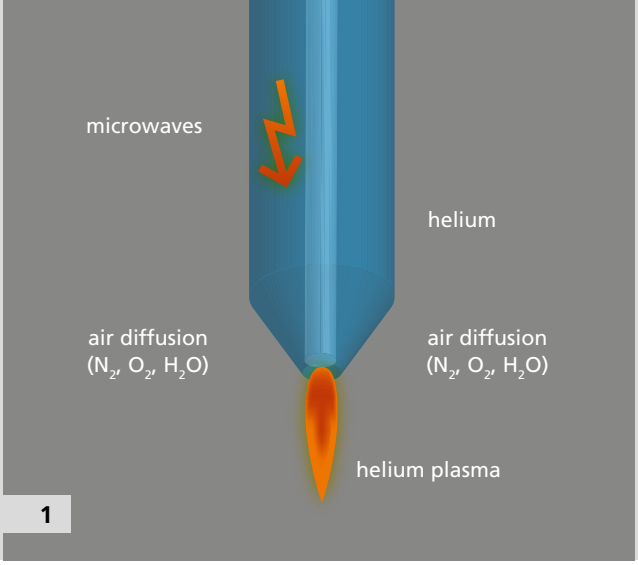

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PROJECTS

PlasmaVac

Therapeutic DNA cancer vaccines are an important alternative to well-known standard treatments in the field of tumor immunotherapy. These DNA vaccines show a stable in vitro expression and a considerable immunological response in cancer patients. As the efficacy of these responses is triggered by the application technique, optimization can further enhance immunotherapies. These application methods include physical, biological and non-biological procedures which have not yet all been tested in clinical studies. The major issues surrounding the application of DNA cancer vaccines are low antigen expression, inefficient cellular migration of the plasmids and inefficient stimulation of the naïve immune system. The main goal of this project is to enhance the efficacy of DNA cancer vaccines with the help of an optimized application technique.

Encapsulating the plasmids through nanoparticles can increase the uptake by dendritic cells and triggers an enhanced, specific plasmid release.

Furthermore, the application of helium plasma has shown a positive response in the enhancement of transfection efficacy and the activation of dendritic cells which form one of the key components in the antigen specific immune response.

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1 *Schematic representation of a helium plasma nozzle.*

1

2

3

LEGASCREEN – Development of an early screening test for dyslexia

Dyslexia is a severe reading and writing disorder, affecting about five percent of all German schoolchildren. It is one of the most common developmental disorders in childhood and youth. Dyslexia is unrelated to the child's intelligence. It results in tremendous problems in school, education, and job. One of the main problems hampering successful therapy is late diagnosis: Using the current methods, dyslexia can be reliably diagnosed at the end of the 2nd grade (7–8 year old children) at the earliest. By this time, a large part of speech-development has already taken place and a lot of precious time for early therapy has inevitably been lost.

Based on our previous research into the genetics of dyslexia, this project aims to overcome such limitations. The earlier a sign of dyslexia is diagnosed, the sooner therapy can be initiated, reducing later problems. LEGASCREEN is a joint project between the Fraunhofer-Gesellschaft and the Max Planck Society. It integrates different research areas, i. e. genetics, morphological (MRI), and functional (EEG) analyses.

Heritability of dyslexia is estimated at between 50 and 70 percent. Genetic information hardly changes during a person's life. Consequently, specific genetic variants can be measured long before reading and writing is taught. Our project will leverage known genetic risk variants as well as further optimizing these genetic markers.

The other important part of the test is based on electro-encephalography (EEG): A procedure which analyzes brain activation without the need for the child´s attention. It is known that even as infants, the brain activation patterns of children who are prone to dyslexia are altered in a certain way in response to specific language stimuli.

Finally, our project also draws on magnetic resonance imaging (MRI). MRI assessments will not be part of the final test procedure, however, they are very helpful during assay development. Information on brain structure provided by MRI can hint at connections between genetics and activation patterns seen in the EEG measures.

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

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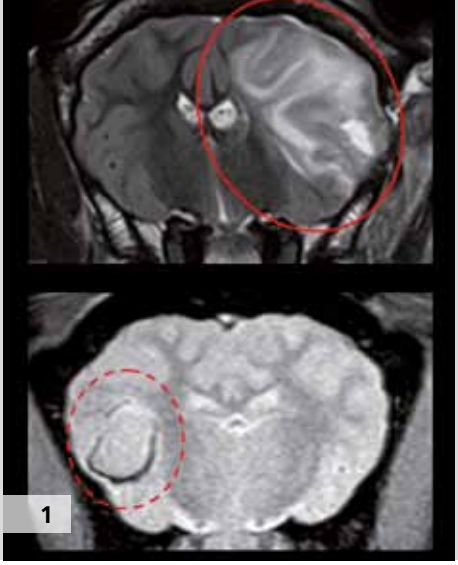
1 *Our aim: Taking pleasure in successful learning.*
2 *EEG examination.*
3 *MRI examination.*



1

Early discrimination between cerebral hemorrhages and ischemia in an ovine model system (ECHO-II)

The only currently approved treatment of acute ischemic stroke is the recanalization of the blocked vessel using alteplase for medicinal thrombolysis. However, this approach is restricted to a narrow time window of 4.5 hours after onset. Cerebral hemorrhage (very similar clinical symptoms) has to be excluded before treatment. At present, a time-consuming imaging procedure is required (e. g. magnetic resonance imaging (MRI), computer tomography (CT)) for differential diagnosis, but is only available in specialized clinics (e. g. stroke units).

To minimize this location and time issue, a new kind of transmittance ultrasound technology is being evaluated in cooperation with SONOVUM AG in a large animal model to enable early diagnosis in acute patients which provides for a rapid and distinct diagnostic assessment. The stroke model in sheep available at our institute serves as a basis for this study. An MRI-based stereotactic procedure was established for implementing a cerebral hemorrhage model. An ultrasound sensor is fixed at the head of a sheep after cerebral hemorrhage or ischemia has been induced. By using the ultrasound measurement, staff are able to distinguish between the two pathologies within 4.5 hours. The diagnosis is verified by means of MRI and necropsy. Furthermore, the evaluation of safe administration after long-term exposure is also being investigated.

Once the transmittance ultrasound technology is established, differential diagnosis would be determined in a matter of minutes or after a couple of hours. Thrombolysis could thus be initiated very early on, resulting in more patients being treated in the future.

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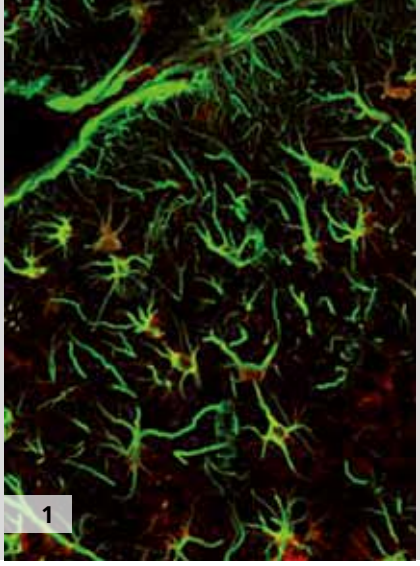
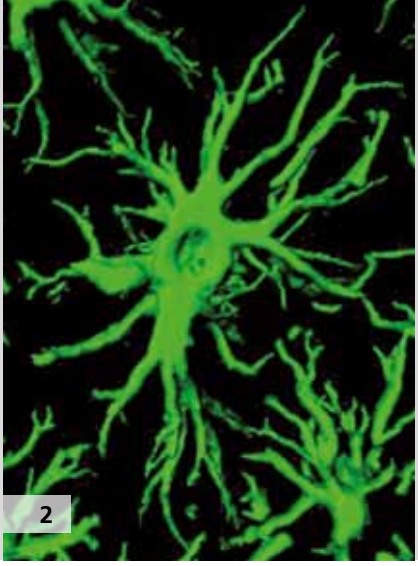
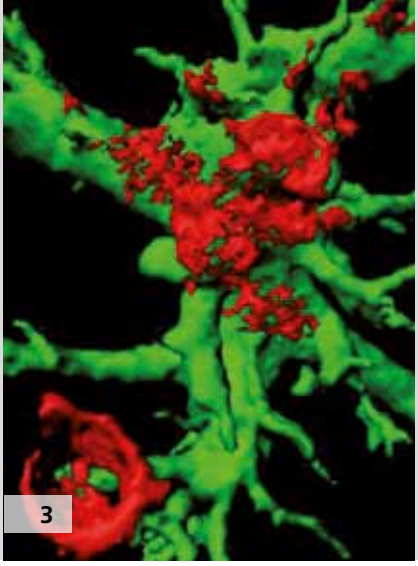
1 *Comparison of cerebral ischemia (top, red circle) and brain hemorrhage (bottom, dashed circle in the MRI).*







Quantification of glial cells following brain tissue damage

Brain tissue damage caused by trauma or hypoxia results in far-reaching changes in the affected areas of the brain. The rebuilding processes do not only affect the vulnerable nerve cells, but also the brain's connective and supporting tissue. These cells, referred to by Rudolf Virchow as glia (Greek for "glue") have extremely varied tasks to fulfill. They surround the nerve cells and provide them with nutrients, thus contribute to the forwarding of information and maintenance of homeostasis in the brain.

Following brain damage, some glial cells experience an enlargement of cells (hypertrophy) and an increase in the number of cells (hyperplasia). This can go so far that it becomes impossible to differentiate between certain glial cells (such as so-called astrocytes) on histological stainings, as they form a tight network of cell bodies and overlapping processes. In spite if this, in order to be able to describe the cells, processes are applied at the Fraunhofer IZI which transform them into definable three-dimensional objects. This makes it possible to quantitatively describe the number of cells, their morphology, interaction with other cells, and their changes over the course of time. For this purpose, the affected tissue is immunohistochemically stained and scanned using confocal laser scanning microscopy. The resulting dataset is processed and rendered into a 3D structure. Overlaps (colocalization) of selectively stained cells can then be projected on top of each other, allowing individual cells and cellular components to be segmented. This allows the subsequent count to determine exactly which segments should be recorded and which should be excluded.

This process enables a precise quantification of pathological changes following brain damage and is, for that reason, suitable for verifying the efficacy of new therapeutic procedures. Additionally, not only the above-mentioned astrocytes, but also any desired cell in any desired histological section can be analyzed. The procedure is currently being adjusted to be able to describe microglial cells and nerve cell interactions in more detail.

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1/2/3 *Immunohistochemical staining of astrocytes (1) and the resulting, rendered 3D models (2) to determine colocalization (3).*

DEPARTMENT OF DIAGNOSTICS

Core competencies of the department

- RNomics
- Biomarker identification
- RNAs as therapeutic targets
- Transcriptome analyses
- Epigenetic investigations
- Molecular diagnostics
- Molecular diagnostic test systems
- Nanotechnology
- Lab-on-a-chip diagnostics
- Tumor stem cells (isolation, characterization and testing)
- Animal models for tumor and chronic inflammatory diseases

A selection of products and services offered by the department can be found on page 51.

IN CONVERSATION WITH PROF. DR. FRIEDEMANN HORN

Since 2011, the department has been coordinating a large project with several Fraunhofer institutes on the development of biomarkers. How is this collaboration work with the involved institutes coming along and which partial results have already been achieved? The collaboration work is for the RIBOLUTION project which is funded by the Fraunhofer Future Foundation. This research alliance, composed of five Fraunhofer institutes, several universities and GlaxoSmithKline, aims to identify and validate new RNA biomarkers which are suitable for the early detection and prognosis of diseases. This includes prostate carcinoma – one of the most common types of cancer. Besides this, the consortium is also concerned with chronic-obstructive pulmonary disease (COPD) which is also widespread and one of the most common causes of death.

Since the beginning of the RIBOLUTION project, a consistently quality-controlled process has been established from clinical sampling to experimental analytics, and a database has been developed where all clinical, experimental and procedural data are recorded and made available. A high number of clinical samples for both diseases have been reviewed and passed on for biomarker identification. In the meantime, over a hundred of these samples have already been examined using genome-wide second generation transcriptome sequencing. The huge volume of data from this sequencing presents the involved bioinformaticians with an exceptional challenge. Initial results, however, already show that a variety of promising, new RNA transcripts have already been found among these data, which are now awaiting validation by means of microarray and RT-PCR analyses. The cooperation between the different consortium partners is working out to be very productive and efficient.

One of the department's major competencies concerns ncRNA technology. What advantages does this technology platform offer and what expectations does it bring with it? Of the 3.3 billion bases of the human genome, only around two per cent are needed to code our repertoire of proteins. The remaining 98 percent were largely considered to be "junk DNA" which had accumulated over the course of evolution but contain no significant information. Research carried out over the past few years, which also involved the RNomics Unit, has however shown that this view was completely naive. These seemingly pointless areas do indeed carry information; they are translated into so-called non-coding RNAs (ncRNAs), of which there is an enormous number in human beings. These ncRNAs form a precise cellular control level and depict the state of a cell much more accurately than other RNAs or proteins. They also represent the pathological state with extreme precision and thus have a great deal of potential as diagnostic biomarkers, e. g. in the diagnosis of tumors or rheumatism. As shown in the above example of microRNAs disabled in prostate cancer, which are also classed among ncRNAs, they are also of great interest from a therapeutic point of view.

Which key research topics does the Department of Diagnostics want to expand over the next few years? Other key research and development topics in the Department of Diagnostics relate to animal models for chronic-inflammatory diseases and tumor diseases. These will be systematically developed over the coming years, as will the highly fascinating field of cancer stem cells for which new therapeutic approaches and innovative analytical methods are urgently required. Another key area is the development of new diagnostic systems. Thanks to Dr. David Smith's efforts to successfully secure an Attract Group, a highly innovative field of nanotechnology, so-called DNA origami technology, will be handled by the department in the coming years.

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UNITS

Inflammation Models and Immunodiagnostics Unit

This unit develops rapid, easy-to-handle, immunological, cell biological and genetic analysis as well as model systems for the areas of graft-versus-host diseases, inflammation research and tumor biology, in particular for articular and pulmonary diseases. Innovative immunoassays, genetic analyses, complex cell culture models and animal experimental approaches are employed here.

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Nanotechnology Unit

The unit is dealing with the development of molecular diagnostic test systems using microspheres and materials in the nanometre field. Using functionalized magnetic particles, a new type of point-of-care diagnostics platform will be developed first and foremost. Nucleic acid-based and protein-based assays will be transferred to this "lab-on-a-chip" module. In addition, the unit is developing different test-strip-based formats, as well as procedures to clean specific nucleic acids effectively. An additional core topic is the use of so-called DNA origami for the nano-functionalization of surfaces.

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RNomics Unit

The RNomics Unit identifies and characterizes disease-associated non-protein-coding RNAs (ncRNAs) for the development of novel diagnostic markers and therapeutic targets. The methods and strategies required for this task are developed by this unit, wherein particular attention is directed to general disease- and system-independent applicability.

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Tumor Stem Cell Unit

This unit's objective is the development of therapeutic strategies based on cells and agents for the treatment of neoplastic diseases on the basis of the elimination or modification of tumor stem cells (TSCs) in the relevant malignant tumor. It is the intention of the concept to describe TSCs of further tumor entities and to facilitate therapeutic innovations in the field of internal oncology.

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1

PROJECTS

Development of a new, epigenetic cancer therapy based on newly synthesized, non-covalent DNMT inhibitors

The degeneration of healthy somatic cells into malignant cancer cells is closely connected to epigenetic changes in the cells' genome. This includes the hypermethylation of so-called tumor suppressor genes through enzymes which are referred to as DNA methyltransferases (DNMT). Unlike genetic mutations, this type of change, however, can, in principle, be reversed and therefore presents a promising approach to the development of new drugs.

The project therefore looks at the design, synthesis and the pharmaceutical development of so-called DNA methyltransferase inhibitors, which intervene in the metabolism of cells and are intended to specifically prevent the hypermethylation of tumor suppressor genes. Besides a specially developed animal model and modern imaging processes, cancer stem cells (CSC) are also used as part of the development.

Cancer stem cells are regarded as germ cells for the formation and growth of tumors. They are equipped with the characteristics typical of stem cells, such as the ability to self-regenerate, or a high differentiation potential. Recent studies allow the assumption that the CSC are particularly resistant to common types of therapy (chemotherapy, radiotherapy) and are therefore responsible for relapses and metastasis. The development of therapy concepts which specifically aim to eliminate CSC is therefore of utmost urgency. The cancer stem cell lines established at the Fraunhofer IZI thus represent an ideal platform for pharmacological development.

As part of the project, the DNMT-relevant target molecules within the CSC-specific signaling pathways are first to be identified and characterized. The DNMT inhibitors identified as being optimal will then be evaluated in a GLP trial on the basis of selected CSC compartments in the animal model. The tumor initiation derived from CSC and the DNMT-based remission of a malignancy can thereby be monitored using bioluminescence imaging. At the same time, the modern imaging procedure allows the entire progress of the disease and therapy within the organism to be observed.

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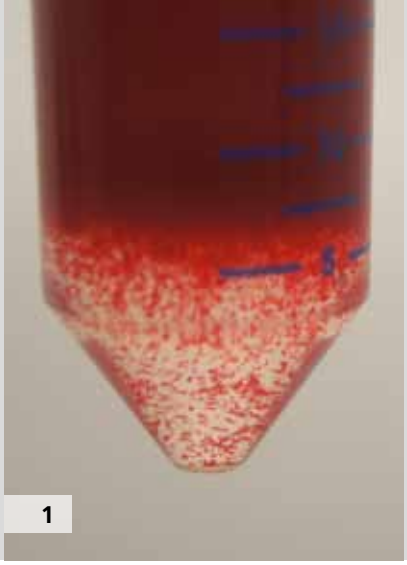
1 *Tumor stem cells.*



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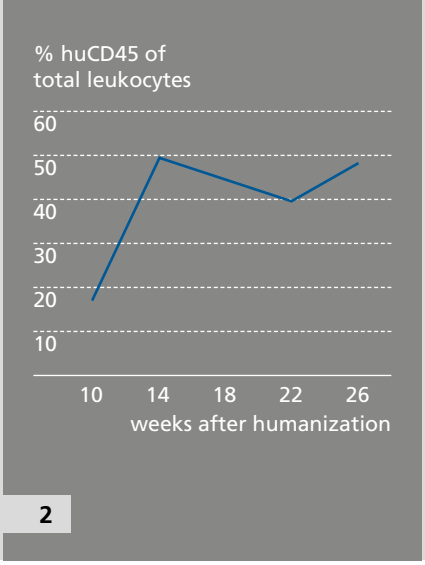

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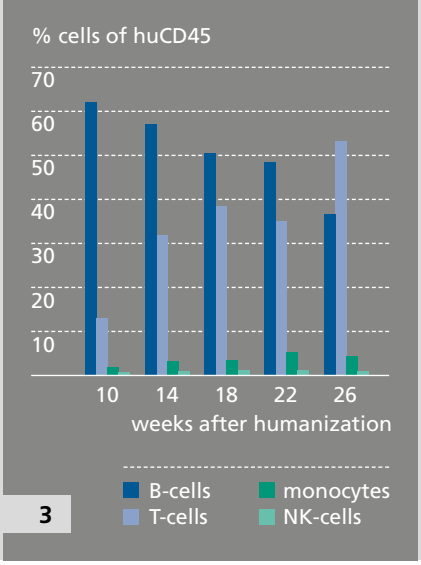

3

Establishing and characterizing the humanized mouse

Animal models have long since been an important instrument in biomedical research. They are used on the one hand in basic research, and on the other for testing new therapeutic agents, thus proving to be essential from an ethical point of view. Nevertheless, it is quite common that the findings resulting from these models are not able to be applied in the human context. For instance, even if a drug has not caused side effects during animal testing, severe side effects may still occur in the case of humans during the clinical testing period. In less serious cases, there is merely a difference between the pathological mechanism that causes a disease in the animal model and the actual human pathological mechanism. In an effort to avoid these inadequacies, the concept of the humanized mouse was developed in the 1980s. This model is based on the idea of recreating a human immune system in a useful format in the laboratory.

The NOD-scid Il2rγ0 mouse strain produces excellent insights into the growth of a human stem cell transplant. These animals are highly immune deficient. The mice are therefore less able to respond to the human stem cells, rendering a rejection of the transplant unlikely. Furthermore, a functional human immune system develops in the mouse from the stem cells which are usually extracted from umbilical cord blood.

In order to determine whether the existing human cells are indeed functional, several parameters are tested. Different, activated immune cells have been found during testing. Moreover, human cytokines and antibodies can be detected. The humanized mouse thus opens up a broad range of research areas. On the one hand, it can be regarded as a contribution to the research of malign tumor diseases and HIV or Dengue virus infections. On the other hand, it can be vital for gaining a new understanding of the symptoms of sepsis. Despite the fact that establishing a new model is an extensive procedure that is dependent upon a number of variables, it offers an excellent opportunity to gain a more comprehensive understanding of human disease mechanisms and will shed light on several topic areas due to its flexible use.

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1 *Human stem cells are obtained from umbilical cord blood. This involves the blood being separated by means of density gradient centrifugation. The first stage of this separation process is shown in the image.*

2 *The proportion of human CD45 (huCD45) increases from week 10 to week 14 and then remains constant with slight variations until the end of the observation period.*

3 *The huCD45 proportion of B-lymphocytes decreases from week 10 onwards, whereas T-lymphocytes increase.*

1

Parodontitis chip

Periodontitis is an inflammatory disease of the gums that, if left untreated, can lead to tooth loss. In Germany alone it is predicted that nearly 12 million people are affected by periodontitis. The main trigger for periodontal disease is bacterial plaque which can lead to a reduction of the dental bone tissue. The postulated systematic relationship between periodontal disease caused by bacterial pathogens and cardiovascular damage has been studied extensively. It can result in particularly serious diseases such as heart attacks and strokes.

The parodontitis chip project is aimed at developing a fully integrated diagnostics platform both for the fast processing and the subsequent analysis of periodontal pathogens in complex samples. This innovative technology consists of a compact microfluidic card and a combined purification module. Steps such as isolating pathogenic nucleic acids, selectively amplifying DNA sequences, and their specific detection are integrated to establish an easy-to-use setup for the end-user.

The lab-on-a-chip device will allow the detection and characterization of 11 bacteria relevant to the pathogenesis of periodontitis in a parallel format. In addition, the establishment of a simple detection unit will allow the monitoring of reaction kinetics. Therefore a quantification of the pathogen, as well as a determination of the total bacterial count can be realized.

The parodontitis chip project will allow for the creation of a simple molecular diagnostic test platform that can easily be adapted to various problems in the field of medical, environmental, or food analysis. Simplified lab-on-chip devices having an extremely simple structure and non-contact detection units provide significant time and cost savings for the user.

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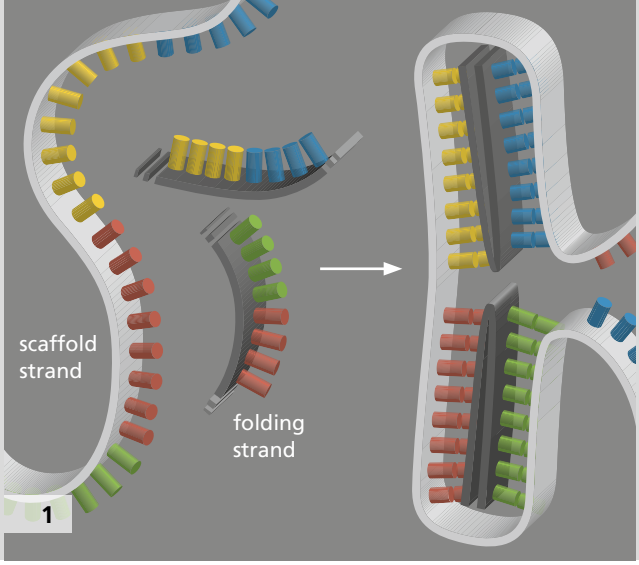
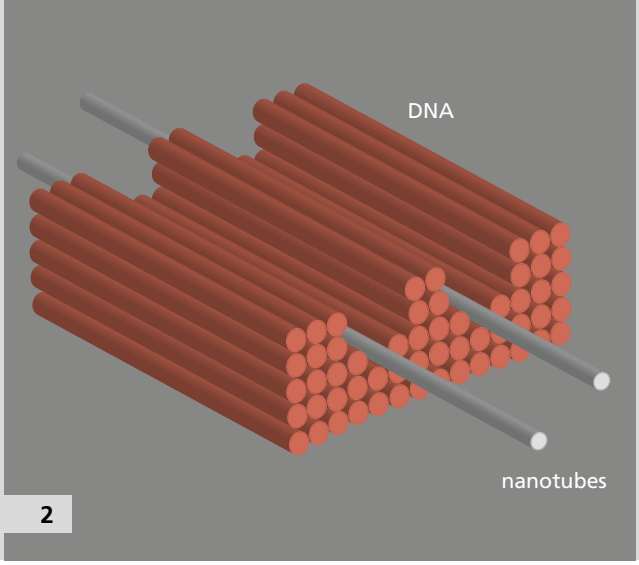
1 *Taking samples for the rapid analysis of periodontal-pathogenic agents using the parodontitis chip.*





DNA origami

Modeled on Japanese paper folding techniques, molecular biological processes which allow DNA molecules to be folded into two and three dimensional structures are referred to as DNA origami. This still very young research field opens up a completely new spectrum of applications in nanotechnology. With the assistance of DNA origami technology, new methods and instruments are available to process materials and molecules in the nanometer range, for which conventional instruments and procedures so far proved to be inadequate. This allows individual molecules or molecule groups to be packed, transported, aligned and positioned. The technology therefore offers new approaches, for example for the coating and functionalization of materials or for transporting active agents. The relatively simple and inexpensive manufacture of DNA origami also promises economic advantages, for example in manufacturing new sensors and developing drugs.

With the self-regulation of complementary base pairs to double-stranded DNA, DNA origami technology is based on simple biophysical processes. Here, single-stranded DNA molecules (scaffold strand) are folded through the connection with short DNA-strands (folding strand), whose base sequence is complementary to defined sections of the scaffold strand (see figure). This allows DNA molecules of a defined size and array to be synthesized and folded at specific points. By doing this, it is possible to construct spatial structures in the smallest of areas and use them for further applications.

An initial application being developed at the Fraunhofer IZI is the alignment of single-walled carbon nanotubes with a diameter of 0.8-2nm and a length of approximately 1 µm, which are of particular significance in the development of biosensors. With the aid of functionalized DNA origami, it will be possible to align and position these nanotubes on a defined surface area. Using this method should drive forward the development of innovative, electronic nano-circuits.

DNA-based nanotechnology offers a variety of additional possible applications in the field of biomedicine. This means that besides sensor development, the smallest amounts of an active agent can be packed and specifically attached to target structures (e. g. to the surface of cancer cells) through targeted modification of the DNA molecules in order to take effect.

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1 *Schematic representation of DNA origami technology.*
2 *Three-dimensional DNA origami with SWNT.*

PRODUCTS AND SERVICES

BUSINESS UNITS

The Fraunhofer Institute for Cell Therapy and Immunology IZI explores and develops solutions to specific problems at the interfaces of medicine, life sciences and engineering. To its clients and partners the institute offers complete solutions ranging from market studies right down to the development of a market-ready product and its marketing authorization. In the business units of drugs, cell therapy, diagnostics / assays and biobanks the Fraunhofer IZI develops, optimizes and validates methods, materials and products for medical, biotechnological and pharmaceutical companies as well as for diagnostic laboratories, hospitals and research facilities. On the following pages please find a list of our special competencies, sorted by departments.

Business Unit Drugs

The development of new therapeutic agents is a time- and cost-intensive process. In many cases there is a gap in the transfer of fundamental research results to clinical practice. The Fraunhofer IZI bridges this gap by means of its special know-how in the field of preclinical development. Our range of services already starts with development services and extends over characterization, optimization and preclinical studies right down to clinical trials. Particular priorities are the development of agents in the fields of oncology, infection biology, autoimmune and inflammatory diseases as well as ischemia.

Business Unit Cell Therapy

Cell therapy is the application of cells or cell suspensions. It is the aim of a cell therapy to induce regenerative processes and to replace dysfunctional or defective cells in the patient, respectively. In order to clinically apply cell therapeutics it is required to demonstrate their safety and effectiveness, which is done in extensive preclinical examinations and clinical trials. The Fraunhofer IZI conducts contract development and testing of cell therapeutic methods. The institute offers all developmental steps from one source, from the design of studies over preclinical development right down to the grant of a manufacturing authorization and the production of test preparations for clinical trials.

Business Unit Diagnostics / Assays

In order to promote the development of regenerative therapy strategies innovative diagnostic methods are required. From the characterization of individual cells to the imaging in living organisms, methods and processes must continuously be adapted and adjusted. The Fraunhofer IZI develops, tests and validates new and adapted diagnostic methods and accompanies its partners until a product has reached market maturity. With innovative methods and new classes of biomarkers (e. g. ncRNA) the institute seeks to develop more sensitive, rapid and cost-effective methods and to transfer them to clinical application.

Business Unit Biobanks

Biobanks are collections of biological material that are stored and optionally preserved in a special manner while providing additional information, e. g. about their origin. Biobanks are established for research and other purposes, e. g. as supply for diagnostic or therapeutic methods or, in the field of biology, for the conservation of biodiversity. As far as human materials are concerned, the donators' consent and specific handling regulations are required.

At the Fraunhofer IZI there are biobanks for various inflammatory and tumor tissues as well as for various types of stem cells, also including tumor stem cells, that serve for the processing of research contracts. The units at the Fraunhofer IZI also develop individual components themselves, like for example new cryoprotectors, and are very experienced in conceiving, establishing, documenting and operating biobanks, which are readily utilized within the scope of contracts.

PRODUCTS AND SERVICES

Department of Cell Engineering

- GMP-compliant development and validation of manufacturing processes
- GMP compliant development and validation of quality controls
- GMP-compliant manufacture of cell therapeutics (advanced therapy medicinal products) for clinical trials
- Antibodies – Monoclonal / polyclonal
- Customized development and validation of immunological in vitro test systems
- Therapy model (mouse) of borreliosis (borrelia burgdorferi)
- Therapy model (mouse) of salmonellosis (salmonella enterica)
- Therapy models (mouse) of chronic inflammatory bowel diseases
- GLP studies (in vitro) – Immunotoxicology, immunogenicity
- GLP studies (in vivo) – Biodistribution, Tumorigenicity, immunotoxicology, immunogenicity
- Validation and beta-evaluation of cell technological procedures / instruments

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Department of Immunology

- Antibody development / characterization
- Assay system to isolate biomarkers in the case of arteriosclerosis / development of plaque
- Determination of the hepatotoxicity of drugs
- Biosensor technology: Cell-based early detection of liver failure
- Development of diagnostic tests for infectious diseases
- Development of defensins and antimicrobial peptides
- Development of diagnostics and therapeutics from peptides
- Enzymatically activatable linker
- Skin transplantation model (mouse)
- Development of vaccines (antigen, expression systems, adjuvants) for human / veterinary medicine
- Vaccine monitoring (development of tests)
- Leukemia model (mouse)
- Human immune system in the animal model (murine)
- Model of inflammatory bowel disease (murine)
- Model of Graft versus Host Disease (in vivo / in vitro)
- Innovative phage-display libraries
- Activation of surfaces (e. g. cell culture)
- Xenogeneic NOD/SCID GvHD mouse model
- Cell / tissue preservation
- Cell separation processes
- Cellular biobanks
- Cellular bioreactors for septicaemia treatment

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Department of Cell Therapy

- Acquisition and evaluation of 3D stacks using confocal laser scanning microscopies
- Development of nucleic acid-based assays
- Development of cell therapy – Alzheimer's
- Establishing stable iPS reporter cell lines
- Experimental imaging
- Genetic-epidemiological analyses
- Large animal model (sheep) for cerebral ischemia
- Histology of the mammal brain
- Model systems myocardial ischemia – rat / mice
- Stroke model systems: Rat / mouse
- Morphological and functional examinations in high-field magnetic resonance imaging
- Optimization of the cryopreservation of cells and tissue
- Quantification of in vivo fluorescence and bioluminescence signals
- Reprogramming of cells – iPS (induced pluripotent stem cells)
- Screening for anti-ageing and tissue-regenerating drugs
- SNP analyses of the human genome
- Spectroscopic examinations in high-field magnetic resonance imaging
- Stereological cell and object analyses
- Testing stem cells in neurodegenerative models
- T-cell infiltration patterns in vitro and in vivo
- Cell sorting
- Center for preclinical studies
- Cytotoxicity assays

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Department of Diagnostics

- Transcriptomic analyses by tilling arrays and ultra high throughput sequencing
- Arthritis models (mice)
- Developing diagnostic rapid tests
- Developing molecular diagnostic detection procedures
- Functional nanoparticles for diagnostics and therapy
- Humanized NSG mouse model
- Cartilage destruction models (mice)
- Microarray analytics
- MicroRNA analytics (expression, localization, targets)
- Allergic rhinitis model (mouse)
- Nanostructuring of surfaces
- Non-coding RNA biomarker
- Non-coding RNA biomarker for oncology, nONCOchip
- Non-coding RNA – therapy targets
- Optimization of pathogen isolation methods
- Personalized tumor killer cells
- Scleroderma model (mouse)
- Cellular functional testing for tissue destructive fibroblasts
- Testing of cytostatics on tumor stem cells (in vitro)
- Cytostatics and cell therapeutics

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EQUIPMENT

With a communicative infrastructure, state-of-the-art laboratory clusters and an extensive equipment pool at hand, the Fraunhofer IZI can offer a broad range of research activities and services.

The institute building

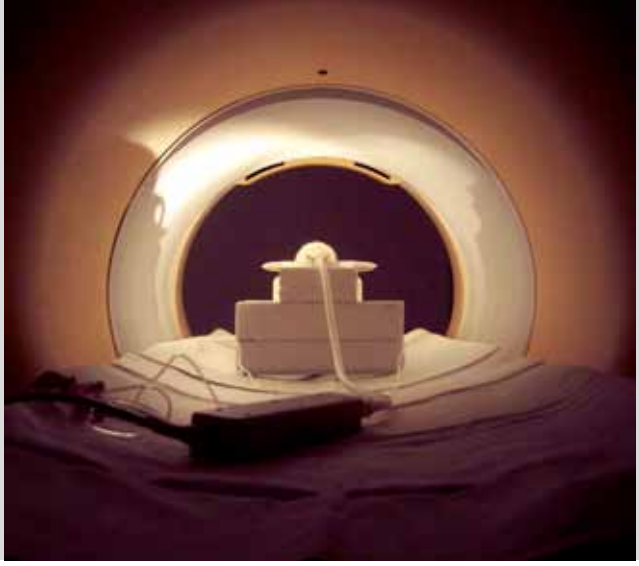
The Fraunhofer IZI consists of two buildings which are connected to each other and also to the neighboring BIO CITY via a total of three bridges. The modern main institute building was completed and put into operation in 2008. The first extension building was completed and moved into in November 2012. As well as excellent working conditions, the buildings offer institute personnel a communicative infrastructure, prompting interdisciplinary exchange between units. A spacious seminar area and a representative atrium in the main building also allow various advanced training formats and scientific events to be carried out, such as the Fraunhofer Life Science Symposium. The first extension building is equipped with laboratories for experimental medicine which cover an area of 1,200 m².

Laboratory capacities

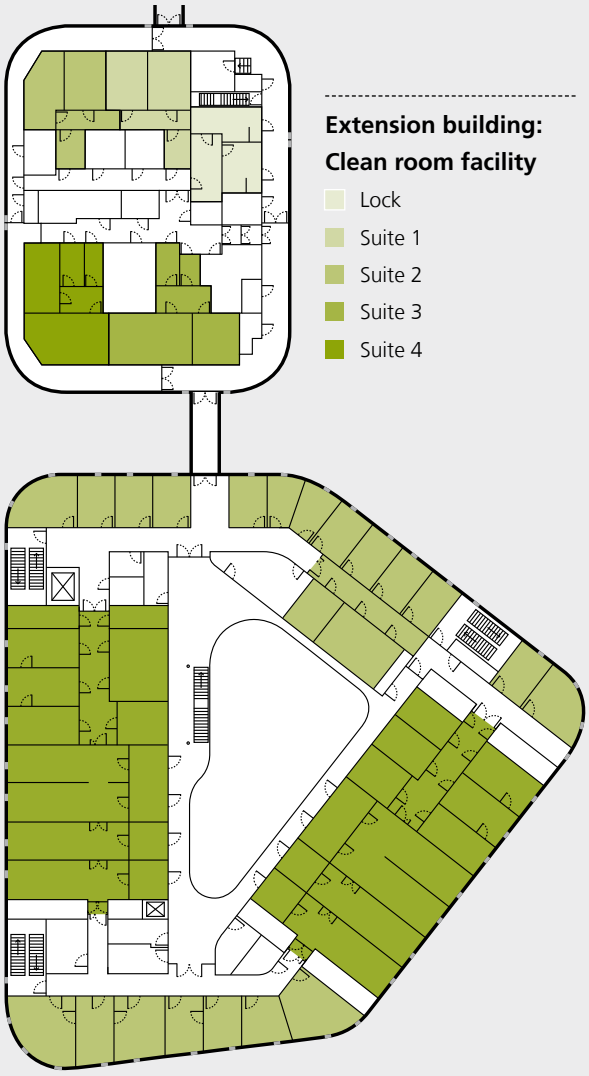
The Fraunhofer Institute for Cell Therapy and Immunology boasts state-of-the-art laboratories. They are particularly well equipped for working in the areas of molecular biology, biochemistry, cell biology and immunology. An extensive immunohistochemistry laboratory, an isotope laboratory, a quality control laboratory with qualified equipment, as well as cyrostorage capacities round off the main building's facilities. The first extension building includes a considerable experimental medicine area which is suitable for establishing and testing small and large animal models. A GMP facility and an expansive equipment pool for all kinds of imaging procedures (e. g. magnetic resonance imaging) complete the research unit. All of the Fraunhofer IZI's laboratories are certified according to S2 standards and therefore suited to work in the fields of genetic engineering and infection biology. A flexible cluster structure allows laboratory sections to be adapted to and fitted in line with the specific requirements of a broad range of projects. The institute occupies a 3 500 m² laboratory area.

Clean room facilities (GMP)

The Fraunhofer IZI operates two clean room facilities with an overall surface area of 900 m². Both facilities are designed for the GMP-compliant manufacture of biopharmaceutical products for clinical trials. The facility is separated into different suites where work can be conducted in line with cleanliness class A. The facility's modular structure allows different projects to be handled in parallel and independently of one another.



Floor plan of the Fraunhofer IZI (3rd floor)



Excerpt of the equipment pool at the Fraunhofer IZI

Cell biological

- Bioreactors (partially automated)
- Flow cytometry
- Cell sorting (e. g. FACS, high-speed)

Molecular biological

- Affinity measurements (BIACORE)
- Automatically optimized purification of proteins (ÄKTA avant)
- Expression analysis system
- High pressure liquid chromatography (HPLC)
- Mass spectrometry
- Microarray scanner and hybridization stations
- Pool of PCR and electrophoresis instruments (e. g. real-time PCR)
- Proteome analytics
- Reporter gene studies (Luminometer)

Imaging

- Bioluminescence imaging
- C-arm X-ray unit
- Fluorescence- / confocal microscopy
- Immunohistochemistry / histology
- 7-tesla small animal magnetic resonance imaging

Others

- Bioinformatics
- BioTechFlow system (simulation of vascular flow)
- DQ / IQ / OQ-qualified equipment for the production of cell therapeutics, therapeutical antibodies and for quality control
- Large animal OP
- In vivo electroporation
- Cryopreservation technology
- Micro surgical instruments

TECHNOLOGY PLATFORMS

With extensive competencies and a state-of-the-art equipment pool the institute is able to offer research services along the entire value chain of a specific technology.

Antibody development

Antibodies identify antigens through a highly specific binding. This makes them interesting tools in biology, medical research and in both treatment and diagnostics.

The Fraunhofer IZI develops and produces antibodies for therapeutic and diagnostic use. Therapeutic antibodies have been mainly used for treatment of different kinds of tumors and lymphomas, treatment of rheumatoid arthritis, Crohn's disease, and asthma, and in the prevention of rejection after organ transplantation.

Antibodies are an essential research tool used in test kits for the detection of soluble or cell-linked marker molecules. They can be modified to change their compatibility or biological characteristics. For in vivo diagnostics as well as functional extension of therapeutic antibodies different methods can be used to link signal and effector molecules.

In order to facilitate tolerance, the Fraunhofer IZI is also developing human monoclonal antibodies with the desired specificities.

Research
- Qualified research and market analysis of a specific field of application
- Identification of competitor products, estimation of the size of a market, detection of market niches and the offering of targeted solutions

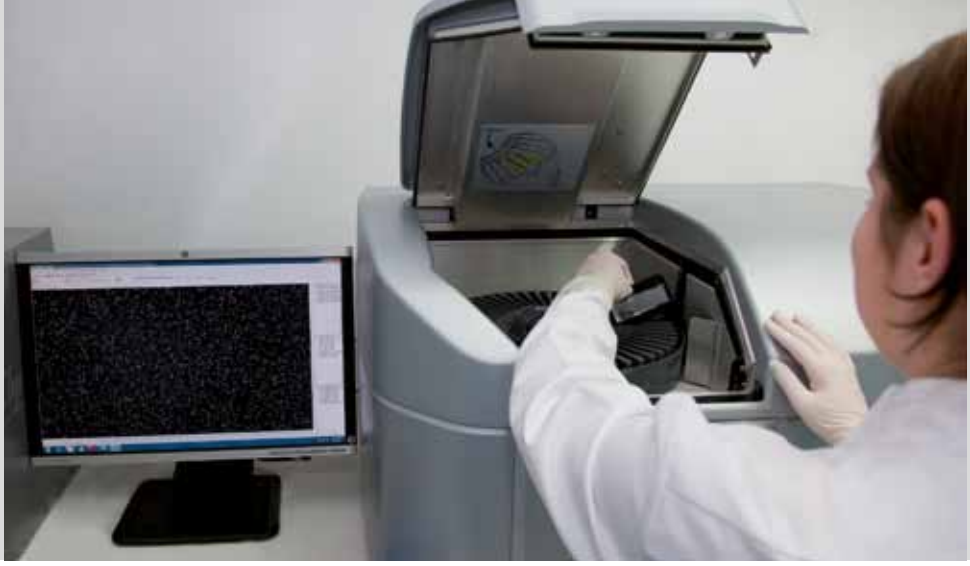
Target indentification
- Identification of target molecules
- Qualification of corresponding epitopes
- Testing of effectiveness in laboratory scale

Production
- Generation and production of polyclonal and monoclonal antibodies
- Optimization through molecular biological methods and / or labelling

Documentation
- GLP conform documentation
- Development of protocols and SOPs

Process development
- Development of a GMP conform production process
- Production of clinical test samples conform with §13 of the German Pharmaceutical Act (AMG)
- Establishment of master- and working cell banks

Clinical trial
- Design and performance of clinical trials (phase II und III) are supported by the institute



Biomarker tests

Biotechnological and biomedical research as well as pre-clinical and clinical trials require validated high throughput analysis methods for detection of biomarkers, drugs and genes. It is important to analyze samples of different origins as rapidly as possible with a high precision. Because customer demands vary widely, the development of a universal test is far away. The Fraunhofer IZI bundles competencies to offer a broad spectrum of analysis methods to its partners.

Therefore existing technology platforms can be combined individually for the seperate requirements of each customer. New analysis methods are then developed in cooperation with the partner. The modern, high-end equipment and the broad competencies of the institute make it a strong partner in assay adaptation and development and screening, of pharmaceutical agents as well as in diagnostics and monitoring. Therefore the complete developmental process, from identification of target molecules to clinical validation of the assay, is represented by the institute.

A unique selling point is the special expertise of the Fraunhofer IZI in RNA technologies. Non-coding RNA (ncRNA) has recently become more important as it can be used as significant biomarkers for either tumor detection or as a new therapeutic target.

Identification of target molecules

- Identification of eligible target proteins or genes associated specifically with a disease

Biomarker development

- Design and synthesis of sensors with high affinity and specificity for a target

Adaption of analytical platforms

- Adaptation of existing (proteomic or genomic) technology platforms for specific assay conditions

Optimizing parameters

- Optimization of the assay in regards to specific sensitivity, speed and costs

Evaluation

- Evaluation of the assay through patient samples in the laboratory according to the gold-standard

Clinical validation

- Validation of the assay with patient samples in clinical environment

Vaccine development

Vaccines and diagnostic assays are elemental methods for combating infectious diseases, in both human and veterinary medicine.

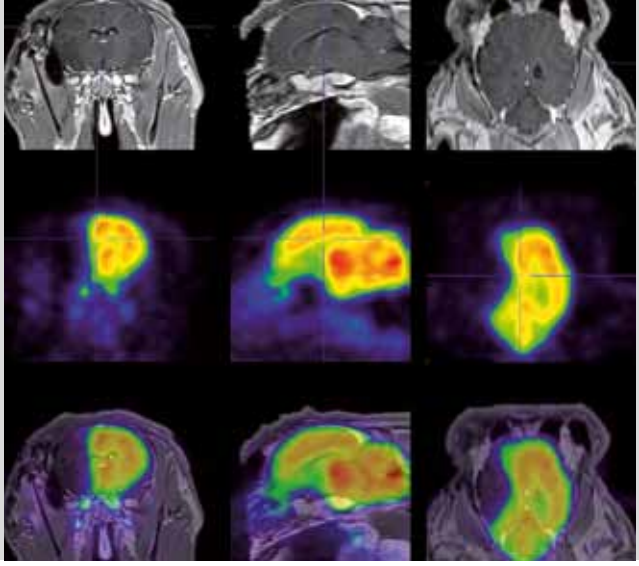
The Fraunhofer IZI's activities in the development of vaccines range from the selection and optimization of suitable antigens right down to the conduct of proof-of-principle tests in various animal models. Pathogens from the fields of virology, bacteriology and parasitology can be processed. Models of ectoparasites (e. g. mites) are also established at the institute.

The Fraunhofer IZI's know-how comprises state-of-the-art vaccine technologies like DNA, recombinant subunit or vector vaccines. In veterinary medicine it is often decisive to distinguish between vaccinated animals and naturally infected animals (DIVA principle, differentiation of infected and vaccinated animal). This is ensured by the methods available at the Fraunhofer IZI.

For the testing of vaccine candidates we have at our disposal small and (due to a close cooperation with the Faculty of Veterinary Medicine at the University of Leipzig) large animal models.

For the serological detection of pathogens the Fraunhofer IZI recombinantly produces antigens which are then optimized for diagnosing by in vitro tests. On the one hand this allows for examining the effectiveness of our vaccine candidates. On the other hand this technology platform offers the possibility to develop novel serological assays (e. g. ELISAs).

- Cultivation of pathogens
- Display of antigens
- Design of vaccine vectors / proteins
- Small animal models for immunizations
- Large animal models for veterinary vaccines
- Characterization of the immune response
- Fine mapping and optimization of epitopes
- Design of accompanying serological assays



Ischemia models

Meaningful model systems are required for the development of therapeutic strategies and diagnostic methods in the field of cerebral and cardiac ischemia. Especially for the prevention of failures and costs in the technology transfer area it is crucial to minimize risks and sources of error already in the course of preclinical development.

The Fraunhofer IZI offers different model systems for addressing a variety of aspects within the development chain. Apart from various in vitro models this also applies to a number of in vivo models. As the transfer of research results from a small animal model to human applications led to a number of failures in the past, a large animal model that is much closer to the human physiology has been developed at the Fraunhofer IZI.

Comprehensive equipment and cooperations in the area of medical imaging have rendered the institute capable of evaluating both regenerative processes and diagnostic applications in vivo.

The institute is particularly specialized in, but not limited to, the development of cell therapeutic methods. Our service portfolio also comprises the testing of agents, surgical therapy methods and the development of new imaging methods.

- Modular design of preclinical studies
- Complete implementation of STAIR criteria
- Adaptation and evaluation of models
- Conduct of studies according to clinical standards
- Monitoring of studies and data management
- Concept assessment and evaluation

Model systems

In vitro models

- e. g. for the identification of neuroprotective effects

In vivo model (rodentia)

- e. g. cell transplantations, behavior analyses, magnetic resonance imaging, histology

In vivo model (ovine)

- e. g. long term studies, utilization of adult autologous stem cell populations, magnetic resonance imaging

QUALITY MANAGEMENT

With a highly successful quality management the Fraunhofer IZI fulfills its clients' and partners' sophisticated demands and thus guarantees research services at the highest level.

GLP – Good Laboratory Practice

"Good Laboratory Practice (GLP) is a quality system concerned with the organizational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported." This is the definition of Good Laboratory Practice in the GLP principles of the Organization for Economic Co-operation and Development (OECD) that were devised following the EC-Directive, which was incorporated into German legislation for chemical compounds ("Chemikaliengesetz"). Good Laboratory Practice, as almost no other quality system, has contributed to health, environmental and animal protection through its worldwide implementation and the consequent widely reciprocal recognition of study data.

Fraunhofer IZI possesses a separate GLP laboratory and trained personnel. These resources are fully equipped to provide integrated research and development solutions.

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GMP – Good Manufacturing Practice

Fraunhofer IZI operates a 450 m^2 GMP-compliant clean room facility. Through the flexible design, the facility is especially attractive for new biotechnology companies that seek to bring newly developed medicinal products into clinical application via clinical trials. The facility is divided into different independent suites. Each has its own grade C clean rooms (preparation), own air locks from grade C to B (personnel and materials transport) 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-based therapeutics (advanced therapy medicinal products). In addition to the clean rooms and the technical infrastructure, the Fraunhofer IZI offers assistance for the set-up and validation of GMP-compliant manufacturing processes as well as for obtaining a manufacturing authorization according to §13 of the German Drug Act (AMG).

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Why are GMP and GLP important?

The clinical trial of new drug candidates is an essential step on the way to approval. Since the 12th revision of the "Arzneimittelgesetz AMG" (German Drug Act) every clinical drug trial must be approved of by the responsible higher federal authority ("Bundesinstitut für Arzneimittel und Medizinprodukte", Federal Institute for Drugs and Medical Devices, Paul-Ehrlich-Institute) and by the responsible ethics commission prior to the initiation of the clinical study. In order to obtain this authorization, the efficacy and safety of the investigational medicinal product must first be verified within the framework of GLP-compliant pre-clinical 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.

GCP – "Good Clinical Practice"

GCP describes internationally accepted regulations which govern the execution of clinical trials. These regulations encompass ethical as well as scientific aspects. Clinical trials are divided into three phases.

- Phase I: Establishment of safety of the new medication/therapeutic
- Phase II: Establishment of the efficacy of the new medication/therapy (Phase IIa) and dose curve (Phase IIb)
- Phase III: Establishment of a significant proof of efficacy (also known as Pivotal-trial).

Only after successful completion of phase III can new substances register for marketing approval. All phases of clinical development must be carried out under the above described GCP-guidelines. The protection of the patient or volunteer must always remain in the foreground. Important aspects of this include the patient consent form, patient trial insurance as well as the exact documentation of the trial results. Additionally GCP regulates the roles of the essential entities involved in the trial including the sponsor, monitor, CRO, primary investigator and ethics committee or intuitional review board and also regulates quality management and adverse event reporting.

The Fraunhofer IZI carries out in cooperation with doctors and SMO's (site management organizations) clinical trials as requested by Sponsors. The Fraunhofer IZI is a reliable partner in the area of clinical trial planning, composition of trial protocols and all other necessary documents required for submission to the regulatory authorities including the ethics committee. Private physicians and SMOs carry out on-site patient visits.

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frank.emmrich@izi.fraunhofer.de

SPIN-OFFS AND COMPANY SETTLEMENTS

The Fraunhofer IZI strengthens the regional economy by helping international and national companies settle in Leipzig and by supporting and encouraging colleagues in starting up their own companies.

Since its foundation in 2005, the Fraunhofer IZI has been substantially involved in the settlement and founding of a total of eleven companies. The attractive subsidies policy of the Free State of Saxony and the on-site support offered by the Fraunhofer IZI were important arguments when it came to partners choosing sites. Together with the newly founded companies, the institute handles projects with a total volume of more than 10 million euros.

Bioville GmbH (founded in 2010)

- Origin: Germany, Fraunhofer IZI
- Business model: Developing and managing projects with a focus on the former trade fair grounds.

Cognate Bioservices GmbH (settled in 2011)

- Origin: USA, Cognate BioServices, Inc.
- Business model: Providing development services for cell therapy products.

InnovaStem GmbH (settled in 2009)

- Origin: Italy, I.M.S. Innovative Medical Solutions S.r.l.
- Business model: Establishing a stem cell bank to store adult stem cells from various neonatal tissues.

Magna Diagnostics GmbH (founded in 2010)

- Origin: Germany, Fraunhofer IZI
- Business model: Developing an innovative diagnostics platform for the rapid diagnosis of infectious diseases based on a lab-on-a-chip system.

MD-5 GmbH (settled in 2012)

- Origin: USA
- Business model: Medical device for stroke therapy.

Northwest Biotherapeutics GmbH (settled in 2011)

- Origin: USA, Northwest Biotherapeutics, Inc.
- Business model: Developing an immunotherapeutic to treat glioblastomas.

Nuvo Research GmbH (settled in 2009)

- Origin: Canada, Nuvo Research Inc.
- Business model: Developing immunomodulatory drugs to treat inflammatory diseases such as rheumatoid arthritis and allergic rhinitis.

Oncotrition GmbH (founded in 2012)

- Origin: Germany, Fraunhofer IZI
- Business model: Nutritional supplement concepts for the prevention of cachexia and the development of tumor-preventative strategies.

Prima BioMed GmbH (settled in 2010)

- Origin: Australia, Prima BioMed Ltd.
- Business model: Developing an immunotherapeutic to treat ovarian cancer.

SelfD Technologie GmbH (settled in 2012)

- Origin: Estonia, Selfdiagnostics, OÜ
- Business model: In vitro diagnostics.

Sonovum AG (founded in 2011)

- Origin: Germany, Fraunhofer IZI
- Business model: Developing diagnostic procedures on the basis of ultrasounds.

PARTNERS

ACOMED Statistik, Leipzig ■ AJ Roboscreen GmbH, Leipzig ■ Alcyomics Ltd., Newcastle, UK ■ ALS Automated Lab Solutions GmbH, Jena ■ AptaIT GmbH, Munich ■ Artcline GmbH, Rostock ■ ASA Spezialenzyme GmbH, Wolfenbüttel ■ Baxter Oncology GmbH, Halle / Westfalen ■ Becit GmbH, Bitterfeld-Wolfen ■ Bombastus-Werke AG, Freital ■ Cognate Bio Services, Inc., Memphis, USA ■ Compart Umwelttechnik GmbH, Weißenfels ■ Cytori Therapeutics Inc., San Diego, USA ■ DMCE GmbH & Co KG, Linz, Austria ■ Dr. med. Steffi Fricke, Specialist in Neurology / Psychiatry / Psychotherapeutic Medicine, Annaberg-Buchholz ■ Entelechon GmbH, Bad Abbach ■ ERT-OPTIK Dr. Thiel GmbH, Ludwigshafen ■ euroderm GmbH, Leipzig ■ FIM Biotech GmbH, Berlin ■ FrimTec GmbH, Oberostendorf ■ Genetic Immunity Kft., Budapest, Hungary ■ Geräte- und Vorrichtungsbau Spitzner OHG, Leipzig ■ GESA Automation GmbH, Teuchern ■ Heat Biologics, Inc., Durham, USA ■ ibidi GmbH, Martinsried ■ IkerChem S.L., San Sebastian, Spain ■ InnovaStem GmbH, Leipzig ■ Isconova AB, Uppsala, Sweden ■ Ixodes AG, Basel, Switzerland ■ Kunststoff- und Elasttechnik GmbH Liegau-Augustusbad, Radeberg ■ Lake Bioscience, Grayslake, USA ■ Magna Diagnostics GmbH, Leipzig ■ MASTERRIND GmbH, Verden ■ Medichema GmbH, Chemnitz ■ microfluidic ChipShop GmbH, Jena ■ Micron Reseach Service, Venturina, Italy ■ Northwest Biotherapeutics, Inc., Bethesda, USA ■ Novartis, Inc., Basel, Switzerland ■ Nuvo Research GmbH, Leipzig ■ PolyBatics, Ltd., Palmerston, New Zealand ■ Praxis PD Dr. Hoheisel, Leipzig ■ Prima BioMed GmbH, Leipzig ■ Prima BioMed Ltd., Sydney, Australia ■ RESprotect GmbH, Dresden ■ Siemens AG, Munich / Erlangen ■ Sonovum AG, Leipzig ■ Vita34, Leipzig

SCIENCE LOCATION LEIPZIG

LEIPZIG AND THE FORMER TRADE FAIR GROUNDS

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

Location: Central for interface partners

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

BIO CITY Leipzig: A potent neighbor

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

Integrated universities

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

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

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

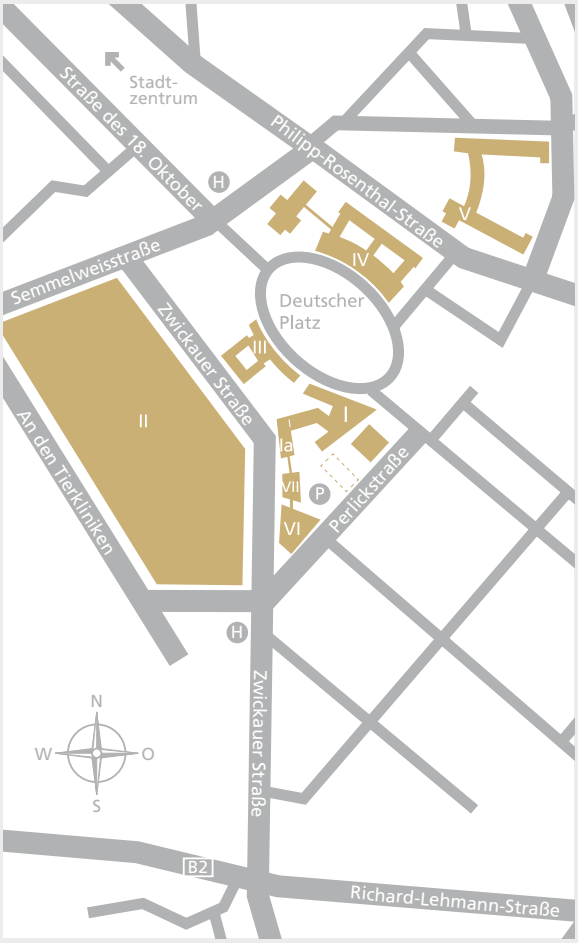
Excellence partner: Translational Center for Regenerative Medicine

One of the most important partners of the Fraunhofer Institute for Cell Therapy and Immunology IZI is the Translational Center for Regenerative Medicine (TRM), which was founded within the framework of the Excellence Initiative 2006 by the German Federal Ministry of Education and Research and the Free State of Saxony. Under the auspices of the renowned immunologist Prof. Dr. Frank Emmrich, institutes from five faculties established the TRM in order to start conceptional, pre-clinical and clinical research projects focused on Tissue Engineering and Materials Sciences (TEMAT), Cell Therapies for Repair and

Replacement (CELLT), Regulatory Molecules and Delivery Systems (REMOD), Imaging, Modeling, and Monitoring of Regeneration (IMONIT). In 2010, the TRM received a very positive evaluation by the consulting firm Capgemini Deutschland Holding GmbH and international consultants, so that funding was granted by the BMBF and Saxony for further support.

Numerous partners in the immediate vicinity

The neighboring partners of the University of Leipzig are, among others, the Translational Center for Regenerative Medicine (TRM) and the University Hospital (special field of transplantation). Further institutions relevant for cooperation are the Heart Center Leipzig GmbH, the Helmholtz Center for Environmental Research (UFZ), the Leibniz Institute for Surface Modification (IOM), the Interdisciplinary Center for Bioinformatics (IZBI), the Center for Clinical Trials Leipzig GmbH (ZKS), the Center for Therapeutic Studies (ZET) and the Leipzig Interdisciplinary Research Cluster of Genetic Factors, Clinical Phenotypes and Environment. Moreover, there are numerous interfaces with different special research areas and so-called Transregios (transregional research projects) that are located in Leipzig.



BIO CITY (I) with hired Fraunhofer IZI area (Ia), Faculty of Veterinary Medicine, institutes and hospitals (II), Max Planck Institute for Evolutionary Anthropology (III), German National Library (IV), Translational Centre for Regenerative Medicine (V), Fraunhofer IZI (VI), extension Fraunhofer IZI (VII).

Translational Centre for Regenerative Medicine (TRM)
Philipp-Rosenthal-Str. 55 | 04103 Leipzig
www.trm.uni-leipzig.de

Interdisciplinary Centre for Clinical Research (IZKF)
Liebigstr. 21 | 04103 Leipzig | www.izkf-leipzig.de

Center for Biotechnology and Biomedicine (BBZ)
University of Leipzig | Center for Biotechnology and Biomedicine | Deutscher Platz 5 | 04103 Leipzig
www.bbz.uni-leipzig.de

University Hospital Leipzig AöR
Liebigstr. 18 | 04103 Leipzig | www.uniklinik-leipzig.de

Heart Center Leipzig GmbH – University Hospital –
Strümpellstr. 39 | 04289 Leipzig
www.herzzentrum-leipzig.de

Coordination Center for Clinical Trials Leipzig (ZKS)
University of Leipzig | Härtelstr. 16–18 | 04107 Leipzig
www.kks.uni-leipzig.de

Interdisciplinary Center for Bioinformatics (IZBI)
University of Leipzig | Härtelstr. 16–18 | 04107 Leipzig
www.izbi.uni-leipzig.de

Max Planck Institutes (MPI)
Max Planck Institute for Human Congnitive and Brain Sciences | Post office box 500355 | 04303 Leipzig
www.cbs.mpg.de

Max Planck Institute for Mathematics in the Sciences
Inselstr. 22 | 04103 Leipzig | www.mis.mpg.de

Max Planck Institute for Evolutionary Anthropology
Deutscher Platz 6 | 04103 Leipzig | www.eva.mpg.de

Helmholtz Center for Environmental Research GmbH – UFZ
Permoserstr. 15 | 04318 Leipzig | www.ufz.de

Leibniz Institute for Surface Modification e.V.
Permoserstr. 15 | 04303 Leipzig | www.iom-leipzig.de

Association for the Advancement of the Health Economics of the Region Leipzig (VGF) e.V.
Deutscher Platz 5a | 04103 Leipzig | www.med-in-leipzig.de

University of Leipzig
Ritterstr. 26 | 04109 Leipzig | www.uni-leipzig.de

Faculty of Medicine
Liebigstr. 27 | 04103 Leipzig | www.medizin.uni-leipzig.de

Faculty of Biosciences, Pharmacy and Psychology
Brüderstr. 32 | 04103 Leipzig | www.uni-leipzig.de/~biowiss

Leipzig University of Applied Sciences (HTWK)
Karl-Liebknecht-Str. 132 | 04277 Leipzig
www.htwk-leipzig.de

Graduate School of Management (HHL)
Jahnallee 59 | 04109 Leipzig | www.hhl.de

EVENTS

THE FRAUNHOFER IZI IN PUBLIC

Events are the key ingredient of the institute's communication strategy. The Fraunhofer IZI once again organized and supported various scientific and public events in 2012.

Long Night of the Sciences
"We quenched the thirst for knowledge!"

On 29 June 2012, over 40 scientific establishments in Leipzig opened their doors for the third Long Night of the Sciences. With over 200 events, members of the general public were offered insights into science which are normally only rarely possible. The Fraunhofer IZI also took part in the event with the slogan "We quench the thirst for knowledge". Around 800 visitors were captivated by the research conducted by members of the institute. Curious visitors were drawn in by the lure of guided tours, hands-on activities and experiments, bringing them closer to the research and development being conducted by Fraunhofer researchers. In the "Science Café", pupils from the Wilhelm-Ostwald-Gymnasium high school discussed the topic of stem cells with researchers. On the initiative of the Fraunhofer IZI, the pupils had independently prepared this discussion forum in the weeks leading up to the event.

Also prior to the event, the Fraunhofer IZI organized the science photo competition "Fascination Microcosmos" together with the Carl-Zeiss Gruppe, which was held for the second time and included all of the Leipzig research institutes. The entries were displayed as part of the Long Night of the Sciences and scored by visitors. The winning photo in 2012 shows a retinal glial cell (Müller cell) and has been used as the cover page for this annual report.

The next Long Night of the Sciences will take place on 27 June 2014.

7th International Symposium on Neuroprotection and Neurorepair

The 7th International Symposium on Neuroprotection and Neurorepair was held from 2–5 May 2012 at the Kongress-hotel in Potsdam. The symposium takes place every two years. Since 2010, Dr. Johannes Boltze, Dr. Alexander Kranz and Dr. Daniel-Christoph Wagner have organized the event together with colleagues from the Otto von Guericke University of Magdeburg and the Leibniz Institute for Neurobiology.

The scientific focus of the event was on neurodegenerative diseases such as stroke, Alzheimer's, dementia and Parkinson's disease, for which there still remains a lack of satisfactory treatment options. Topics covered innovative, therapeutic and diagnostic approaches, predominantly relating to clinical practicability. Over 40 of the most internationally renowned experts in these highly topical fields presented their current research findings, while young scientists also had the opportunity to present their work. Over 300 colleagues from 29 countries took part in the event and discussed the newest findings across over 180 contributions.

The 8th International Symposium on Neuroprotection and Neurorepair will take place from 9–12 April 2014 in Magdeburg.

The Fraunhofer Innovation Forum on Demography + Health Resources

The Fraunhofer Innovation Forum "Demography and Health Resource" took place for the third time on 1 and 2 November 2012 at the Fraunhofer IZI. The event format is organized by eVAA e.V. and has been bringing together decision makers from national and international business, politics, education and research since 2008 to discuss the implications of demographic change with regard to the health sector. Professor Emmrich opened and hosted the event.

This year, two topics were focused on in plenary sessions and workshops: On the one hand there was a discussion of projects and studies serving as models, which target a need-based and economical care structure. This includes effective disease management and sustainable health concepts that cater to the rising average age of the population. A second core topic addressed people as our most important economic resource. Capabilities, opportunities and the added value of innovations from regenerative medicine, health management and gerontology were presented and discussed. Programs and models were also discussed which could guarantee vitality and productivity in the long-term, also in older age.

International Symposium of the German Society for Cell Biology "Molecular concepts in epithelial differentiation, pathogenesis and repair"

The Fraunhofer IZI hosted an international meeting of the German Society for Cell Biology (DGZ) from 7–10 November 2012. The society aims to support research into cell biology and also to establish the field as an independent university subject.

The meeting's scientific spotlight was on epithelial differentiation as well as pathogenesis and repair mechanisms. Around 140 international participants discussed foundations of cell biology, immunological aspects and therapeutic concepts regarding the regeneration of epithelia. Besides numerous scientific presentations and a poster display, guests could also enjoy an exciting social program including a visit to the Saint Nicholas Church and the BMW factory.

Girls' Day at the Fraunhofer IZI

Getting girls and women interested in scientific and technical careers is the main aim of the nationwide Girls' Day. The Fraunhofer IZI took part in this event for the first time on 26 April 2012. By means of talks and a mini lab internship, visitors were able to find out about the institute's research topics and career opportunities at the Fraunhofer-Gesellschaft and experience the profession of science up close.

The next Girls' Day will take place on 25 April 2013.

LOOKING TO 2013

25 April 2013
Girls' Day 2013
Girls and women are once again invited to discover exciting occupational fields in biomedical research as part of this year's Girls' Day. Female members of staff at the Fraunhofer IZI will speak about their professional experience and personal development paths.
www.girls-day.de

23–25 October 2013
World Conference on Regenerative Medicine 2013
The World Conference on Regenerative Medicine brings together researchers, medics and companies for an exchange focused on the interdisciplinary research fields of regenerative medicine. Besides stem cell research, this also covers the areas of cell therapy, biomaterials, tissue engineering and immunological issues.
www.wcrm-leipzig.com

24 October 2013
Fraunhofer Life Science Symposium "Automated Cell Manufacturing"
This year, the Fraunhofer Life Science Symposium will look at automation processes in the manufacture of cell and tissue products. In 2013, the symposium will be integrated into the World Conference on Regenerative Medicine as a satellite program.
www.fs-leipzig.com

SCIENTIFIC PRESENCE

CONVENTIONS AND CONFERENCES

118th Congress of the German Society for Internal Medicine (oral presentation), April 14–17, 2012, Wiesbaden, Germany

11th International Symposium "Molecular Basis of Pathology and Therapy in Neurological Disorders" (oral presentation), November 22–23, 2012, Warsaw, Poland

11th Leipzig Research Festival for Life Sciences 2012 (poster presentation / attendee), December 14, 2012, Leipzig, Germany

13th International Symposium Albumin Dialysis (oral presentation), September 28, 2012, Rostock, Germany

15th Annual Meeting of the European Society for Clinical Virology (ESCV) (attendee), September 4–7, 2012, Madrid, Spain

18th International Conference on DNA Computing and Molecular Programming (attendee), August 14–17, 2012, Aarhus, Denmark

2nd Fraunhofer Strategy Seminar 2012 (attendee), November 19–20, 2012, Berlin, Germany

2nd Infectious Medicine Symposium for Central Germany – Young academics research – (poster presentation), September 10, 2012, Leipzig, Germany

2. IQUO Congress (Interest Group for the Qualitäty Assurance of the Work of Resident Uro-Oncologists in Germany) (oral presentation), June 29–30, 2012, Berlin, Germany

2012 BIO International Convention (info booth), June 18–21, 2012, Boston, USA

20th World Congress of Psychiatric Genetics (attendee), October 14–18, 2012, Hamburg, Germany

22nd Annual Meeting of the Society for Virology (poster presentation), March 14–17, 2012, Essen, Germany

2nd Korea-Germany International Joint Symposium (oral presentation), October 5–8, 2012, Gwangju, South Korea

30th German Cancer Congress (orla presentation), February 22–25, 2012, Berlin, Germany

32nd ISICEM – International Symposium on Intensive Care and Emergency Medicine (oral presentation), March 20–23, 2012, Brussels, Belgium

39th ESAO Congress of the European Society for Artificial Organs (ESAO) (oral presentation), September 26–29, 2012, Rostock, Germany

3rd International Conference "Strategies in Tissue Engineering" (info booth), May 23–25, 2012, Würzburg, Germany

4th KKSN Symposium 2012 (oral presentation / chair / scientific advisory council), March 22–23, 2012, Berlin, Germany

4th European Veterinary Immunology Workshop (poster presentation), September 2–4, 2012, Edinburgh, UK

5th Biosaxony on-site "Biotechnology and Food Technology" (attendee), October 11, 2012, Radeberg, Germany

50th Annual Meeting of the German Society for Nuclear Medicine (oral presentation), April 25–28, 2012, Bremen, Germany

55th Annual Meeting of the Germany Society for Veterinary Medicine and 17th Pathology Seminar: Pathology of Spontaneous Diseases of Rodant Laboratory Animals (poster presentation), March 9–11, 2012, Fulda, Germany

6th Leipzig Veterinarian Congress (oral presentation), January 19–21, 2012, Leipzig, Germany

63rd Annual Conference of the International Dyslexia Association (oral presentation), October 24–27, 2012, Baltimore, USA

7th Fraunhofer Life Science Symposium (poster presentation / attendee), November 29–30, 2012, Leipzig, Germany

7th International Symposium on Neuroprotection and Neurorepair (poster presentation), May 2–5, 2012, Potsdam, Germany

8th Fraunhofer EU-NetWorkshop (attendee), April 19–20, 2012, Dresden, Germany

8th International Congress on Autoimmunity (poster / oral presentation), May 9–13, 2012, Granada, Spain

8th World Stroke Conference (poster presentation), October 10–13, 2012, Brasilia, Brasil

9th International Congress of Veterinary Virology (attendee), September 4–7, 2012, Madrid, Spain

Business Meeting Neuro Intensive Care and Emergency Medical Aid 2012 (attendee), January 18–21, 2012, Berlin, Germany

Archamps Technopole Meeting (oral presentation), September 14, 2012, Archamps, France

BIO-Europe 2012 (attendee), November 12–14, 2012, Hamburg, Germany

BIO-Europe Spring 2012 (attendee), March 19–21, 2012, Amsterdam, The Netherlands

BioJapan 2012 World Business Forum (attendee), October 10–12, 2012, Yokohama, Japan

Cooperation Forum Cell-based Therapies 2012 (attendee), March 27, 2012, Erlangen, Germany

ESAO Winter School 2012 (oral presentation), February 2–4, 2012, Catania, Italy

European Congress of Immunology (poster presentation), September 5–8, 2012, Glasgow, UK

Fraunhofer Symposium "Netzwert" (oral presentation / attendee), December 4–5, 2012, Munich, Germany

Joint Annual Meeting of the German, Austrian, and Swiss Societies for Hematology and Oncology (oral presentation), October 19–23, 2012, Stuttgart, Germany

ImmunoTrends (oral presentation), December 17, 2012, Berlin, Germany

International Sympsoium – The Neutrophil in Immunity 2012 (oral presentation), June 9–12, 2012, Quebec, Canada

International Stroke Conference 2012 (attendee), February 1–3, 2012, New Orleans, USA

International Symposium for Anesthesia, Intensive Therapy, Emergency Medical Aid, and Pain Therapy (oral presentation), January 28–February 3, 2012, Sankt Anton, Austria

Annual Meeting of the German Working Group for Chronic Inflammatory Bowel Diseases (oral presentation), June 22–23, 2012, Mainz, Germany

Annual Meeting of the German Society for Medical Informatics, Biometrics and Epidemiology (oral presentation), September 16–21, 2012, Braunschweig, Germany

RESEARCH PARTNERS

NanoRegen Mission to Germany & Austria (oral presentation), September 4–7, 2012, Leipzig, Germany

science meets companies 2012 (info booth), May 9, 2012, Halle, Germany

Symposium on Zoonoses Research (poster presentation), October 11–12, 2012, Berlin, Germany

The GRDC Symposium 2012 (oral presentration), November 12–13, 2012, Seoul, South Korea

VII International Symposium on Antimicrobial Resistance (attendee), February 29–March 2, 2012, Cartagena, Columbia

World Immune Regulation Meeting-VI (poster presentation), March 18–21, 2012, Davos, Schwitzerland

World Stem Cell Summit 2012 (oral presentation / chair), December 3–5, 2012, West Palm Beach, USA

XXX Congreso Anual de la Sociedad Espanola de Ingenieria Biomedica (CASEIB2012) (oral presentation), November 19–21, 2012, San Sebastian, Spain

AIT Austrian Institute of Technology, Department of Heath and Environment, Vienna, Austria

Biomedical Primate Research Centre, Department of Virology, Rijkswijk, The Netherlands

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

Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Medical Department, Division of Hematology, Oncology, Berlin, Germany

Chonnam National University, Gwangju, South Korea

Ernst Moritz Arndt University Greifswald, University Hospital, Institute for Immunology and Transfusion Medicine, Greifswald, Germany

Flensburg University of Applied Science, Department of Biotechnology and Process Engineering, Flensburg, Germany

Research Center Borstel, Leibniz Center for Medicine and Biosciences, Borstel, Germany

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

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

Fraunhofer Institute for Electronic Nano Systems ENAS, Chemnitz, Germany

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

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

Fraunhofer Institut for Ceramic Technologies and System IKTS, Dresden, Germany

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

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

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

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

Fraunhofer Institute for Mechanics of Materials IWM, Business unit Biological and macromolecular materials, Halle, Germany

Fraunhofer Institute for Reliability and Microintegration IZM, Berlin, Germany

Freie Universität Berlin, Department of Veterinary Medicine, Berlin, Germany

Ghent University, Faculty of Veterinary Sciences, Laboratory for Gene Therapy, Gent, Belgium

Helmholtz Center for Environmental Research UFZ, Department Environmental Microbiology | Department Proteomics | Department Environmental Immunology, Leipzig, Germany

Herzzentrum Leipzig GmbH (Heart Center Leipzig), Clinic for Cardiology, Leipzig, Germany

Leipzig University of Applied Science, Faculty of Electrical Engineering and Information Technology, Leipzig, Germany

Furtwangen University, Faculty for Manufacturing Systems Engineering and Process Engineering, Villingen-Schwenningen, Germany

Karolinska Institut, Department of Medicine, Solna, Stockholm, Sweden

Clinic St. Georg gGmbH, Robert Koch Clinic, Leipzig, Germany

Leibniz Institute of Surface Modification, Leipzig, Germany

Ludwig Maximilians University Munich, Faculty of Veterinary Medicine, Munich, Germany

Pilot Pflanzöltechnologie Magdeburg e.V., Magdeburg, Germany

Polish Academy of Sciences, Centre for Molecular and Macromolecular Studies, Department of Engineering of Polymer Materials, Łódź, Poland

Radboud University Nijmegen, Faculty of Science, Institute for Molecules and Materilas, Bio-organic Chemistry, Nijmegen, The Netherlands

Saxon State Office for Environment, Agriculture, and Geology, Dresden, Germany

Seoul National University, NANO Systems Institute, Seoul, South Korea

St. Elisabeth Clinic Leipzig, Academic Teaching Hospital of the University of Leipzig, Department for Urology | Senology / Breast Center, Leipzig, Germany

Stanford University, School of Medicine, Department of Neurosurgery, Stanford, USA

University of Leipzig, Center for Biotechnology and Biomedicine | Faculty for Biosciences, Pharmacy and Psychology | Faculty of Medicine | Faculty of Medicine, Medical Experimental Center | Translational Center for Regenerative Medicine (TRM) | Translational Center for Regenerative Medicine (TRM), Research Area CELLT – Cell Therapies for Repair and Replacement | Faculty for Veterinary Medicine | Faculty for Veterinary Medicine, Large Animal Clinic for Theriogenology and Ambulatory Services | Faculty for Veterinary Medicine, Animal Surgery Clinic | Faculty for Veterinary Medicine, Institute for Veterinary Pathology | Faculty for Veterinary Medicine, Bird and Reptile Clinic | Faculty for Veterinary Medicine, Institute for Veterinary Anatomy, Leipzig, Germany

University of Regensburg, Faculty for Medicine, Regensburg, Germany

University of Rostock, Faculty for Medicine, Institute for Transfusion Medicine, Rostock, Germany

University of Salzburg, Priority Program BioScience and Health, Salzburg, Austria

University of Zurich, Vetsuisse Faculty, Institute for Laboratory Animals, Zurich, Switzerland

Saarland University Medical Center, Clinic for Tooth Preservation, Parodontology and Preventive Dentistry, Homburg / Saar, Germany

University Clinic Greifswald, Clinic and Polyclinic for Neurology, Greifswald, Germany

University Clinic Leipzig, Department for Imaging and Radiation Medicine, Division of Neuroradiology | Department for Imaging and Radiation Medicine, Clinic for Radiation Therapy and Radiooncology | Department for Imaging and Radiation Medicine, Clinic and Polyclinic for Nuclear Medicine | Department for Diagnostics, Institute for Clinical Immunology and Transfusion Medicine | Department for Diagnostics, Institute for Medical Microbiology and Infection Epidemiology | Department for Diagnostics, Institute for Pathology | Department for Diagnostics, Institute for Virology | Department for Internal Medicine, Neurology and Dermatology, Division for Hematology and Internal Oncology | Department for Internal Medicine, Neurology and Dermatology, Clinic and Polyclinic for Dermatology, Venerology and Allergology, Research Group Skin | Department for Internal Medicine, Neurology and Dermatology, Clinic and Polyclinic for Gastroenterology and Rheumatology | Department of Ophthalmology | University Gynecological Clinic, Leipzig, Germany

Universitäty Clinic Münster, Clinic and Polyclinic for Neurology, Münster, Germany

Universitäty Clinic Regensburg, Institute for Immunology | Institute for Clinical Chemistry and Laboratory Medicine | Clinic and Polyclinic for Internal Medicine I, Division Rheumatology and Clinical Immunology | Clinic and Polyclinic for Radiation Therapy | Center for Internal Medicine, Clinic II, Division for Gastroenterology, Rostock, Germany

University Medical Center of the Johannes Gutenberg University Mainz, Institute for Microscopic Anatomy and Neurobiology, Research Group Molecular Imaging and Optogenetics, Mainz, Germany

University of Padova, Department of Molecular Medicine, Padua, Italy

University of Thessaloniki, Medical School, Thessaloniki, Greece

Urological Practice & Study Institute Dr. Schulze, Markkleeberg, Germany

Washington University, School of Medicine, Division of Infectious Diseases, St. Louis, USA

ADVANCED VOCATIONAL TRAINING

8th Spring School on Immunology, German Society for Immunology (DGfI), Ettal, Germany

Advance imaging course, BRUKER BioSpin GmbH, Ettlingen, Germany

Advanced presentation skills, University of Leipzig, Research Academy Leipzig, Leipzig, Germany

Allergological and infectiological issues in doctors' practices and in hospitals, Prof. Dr. Hoheisel, Leipzig, Germany

Doctor-patient seminar, Deutsche Morbus Crohn / Vereinigung DCCV (German Crohn's disease / ulcerative colitis self-help association), Hamburg, Germany

Biostatistics, University of Leipzig, Translational Center for Regenerative Medicine (TRM) Leipzig, Leipzig, Germany

DEGUM ultrasound advanced training course, University Clinic Leipzig, Leipzig, Germany

Flow Cytometry, MACSQuant Analyzer, Miltenyi Biotec GmbH, Leipzig, Germany

ESAO Winter School, European Society for Artificial Organs, Catania, Italy

EU project management, EU Office of the BMBF, PT-DLR, Berlin, Germany

Medical specialist training: Internal medicine, section central emergency hospitalization, intensive care, University Clinic Leipzig, Leipzig, Germany

FACS crash course, Becton Dickinson GmbH, Heidelberg, Germany

Falk Symposium 183 – Dealing with our "In-vironment": New aspects in IBD pathogenesis and therapy, International Falk Symposia and Workshops, Basel, Switzerland

Advanced training for investigators, KKS-Network, Leipzig, Germany

Fraunhofer summer school: R&D marketing, Fraunhofer Marketing Network, Berlin, Germany

Seminar for managerial staff, windwerker | human performance factory GmbH, Leipzig, Germany

Fundraising for young scientists, University of Leipzig, Competence School ELSYS, Research Academy Leipzig, Leipzig, Germany

GLP course, ACPS – Applied Clinical Pharmacology Services / Nuvo Research GmbH, Leipzig, Germany

GLP course, University of Leipzig, Translational Center for Regenerative Medicine (TRM) Leipzig, Leipzig, Germany

GLP training course, Klinkner & Partner GmbH, Leipzig, Germany

Good distribution practice "Logistic challenges in stem cell technology and regenerative Medicine", World Courier (Deutschland) GmbH, Leipzig, Germany

Good distribution practice "Training for processing of transports in multicentrical clinical trials", World Courier (Deutschland) GmbH, Leipzig, Germany

Basic course laboratory animal science, University of Leipzig, Faculty of Medicine, Medical Experimental Center, Leipzig, Germany

Compact course "Experimental animals, animal experiments and alternative methods" Felasa B, Berliner Kompaktkurse, Berlin, Germany

Managing manufacturing, Concept Heidelberg GmbH, Mannheim, Germany

Managing quality control, Concept Heidelberg GmbH, Heidelberg, Germany

Supplier qualification, PTS Training Service, Wiesbaden, Germany

Control of measuring and test devices: Mass, volume, temperature, Klinkner & Partner GmbH, Saarbrücken, Germany

"International science policy" module, University of Leipzig, Research Academy Leipzig, Leipzig, Germany

"Key competences" module, University of Leipzig, Research Academy Leipzig, Leipzig, Germany

Biomolecular methods, Thermo Fisher Scientific, Leipzig, Germany

Navios flow cytometry course, Beckman Coulter GmbH, Krefeld, Germany

Nucleic acid purification, MACHEREY-NAGEL GmbH & Co. KG, Leipzig, Germany

Optimization of cloning, optimization of reverse transcription and PCR as well as Western blot analyses, Thermo Fisher Scientific, Leipzig, Gemany

Quality aspects in the manufacture of ATM, BioTOP Berlin-Brandenburg, BB-Life Seminars, Berlin, Germany

Quality control in flow cytometry, Beckman Coulter GmbH, Leipzig, Germany

TEACHING ACTIVITIES

Quality assurance in analytical laboratories, Karlsruhe Institute of Technology, Karlsruhe, Germany

Real time PCR, Roche Diagnostics Deutschland GmbH, Leipzig, Germany

Legal and financial aspects of FP7, EU office of the BMBF, PT-DLR, Bonn, Germany

Training session for scientific personnel on handling experimental animals with respect to animal welfare, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany

Seminar RNA tools, siRNA / shRNA, Thermo Fisher Scientific, Leipzig, Germany

Sepsis workshop, 64th Annual Meeting of the German Society for Hygiene and Microbiology, Hamburg, Germany

Statistics one, Princeton University, online

Animal experiment FELASA compact course C, Berlin compact course, Berlin, Germany

Lecture series human genetics, University of Leipzig, Institute for Human Genetics, Leipzig, Germany

Leipzig University of Applied Science:
Microfluidics and dosing systems (lecture / talk)

University of Leipzig:
Acute leukaemia (course), chemistry for medical practitioners (seminar), introduction to clinical medicine (course), basics of immunology (lecture), core lecture on immunology (lecture), immunological methods (lecture), immunological practical training for medical practitioners (practical training), infectiology and immunology (problem-oriented learning), learning and behavioral disorders (lecture), lymphomas (course), medicine of the ageing individual (problem-oriented learning), medical biotechnology / regenerative medicine (lecture), monoclonal antibodies – manufacturing and application (lecture), novel technologies in vaccine development (lecture), QSB tissue typing (seminar), QSB transfusion medicine (seminar), QSB environmental medicine (seminar), QSB10 prevention and health promotion (lecture), QSB4 infectiology / immunology (lecture), elective in medical biotechnology / regenerative medicine (lecture)

University of Rostock:
Gastrointestinal immune system (seminar), core lecture on anesthesiology and intensive therapy (lecture), core lecture on internal medicine / nephrology (lecture), degree course in biomedical engineering (lecture), degree course in biomedical engineering (seminar), elective in anesthesia (lecture)

EVALUATOR ACTIVITIES

Acta Neurobiologiae Experimentalis, Dr. Daniel-Christoph Wagner

American Journal of Kidney Diseases, Prof. Dr. Steffen Mitzner

Artificial Organs, Dr. Daniel-Christoph Wagner, Prof. Dr. Frank Emmrich

BMC Medical Genetics, Dr. Holger Kirsten

BMC Neuroscience, Dr. Daniel-Christoph Wagner

Brain Research Bulletin, Dr. Daniel-Christoph Wagner

British Journal of Nutrition, Peggy Bodammer

Cardiovascular Research, Dr. Claus Kerkhoff

Cell Biology and Toxicology, Martin Sauer

Cell Communication and Signaling, Dr. Claus Kerkhoff

Cellular and Molecular Life Sciences (CMLS), Prof. Dr. Frank Emmrich

Critical Care Medicine, Prof. Dr. Steffen Mitzner

ASSOCIATION MEMBERSHIPS

Cytotherapy, Dr. Daniel-Christoph Wagner

Experimental Dermatology, Dr. Claus Kerkhoff

Future Drugs – Expert Reviews Vaccines, Dr. Jörg Lehmann

Hepatology, Prof. Dr. Steffen Mitzner

International Journal of Biochemistry & Cell Biology, Dr. Claus Kerkhoff

International Journal of Cancer, Dr. Claus Kerkhoff

International Journal of Pharmaceutics, Dr. Sebastian Ulbert

Intervirology, Dr. Sebastian Ulbert

Journal of Immunology, Dr. Claus Kerkhoff

Kidney International, Prof. Dr. Steffen Mitzner

Mediators of Inflammation, Dr. Claus Kerkhoff

PLoS One, Dr. Claus Kerkhoff, Dr. Daniel-Christoph Wagner

The Open Veterinary Science Journal, Dr. Jörg Lehmann (Editorial Board)

Therapeutic Apheresis and Dialysisis, Martin Sauer

Vaccine, Dr. Sebastian Ulbert

Veterinary Immunology and Immunopathology, Dr. Jörg Lehmann

American Heart Association, Dr. Alexander Deten, Dr. Alexander Kranz

American Society of Biochemistry and Molecular Biology (ASBMB), Dr. Claus Kerkhoff

American Stroke Association, Dr. Alexander Kranz

Study-group for experimental stem cell transplantation, Dr. Stephan Fricke

Doctors for Madagaskar, Prof. Dr. Frank Emmrich

Association for Cancer Immunotherapy (CIMT), Christopher Oelkrug

Biosaxony e. V., Prof. Dr. Frank Emmrich (board member)

German Society for Gerontology (DGfA), Dr. Alexandra Stolzing

German Society for Anesthesiology and Intensive Care (DGAI), Martin Sauer

German Society for Epidemiology (DGEpi), Dr. Holger Kirsten

German Society for Gerontologie and Geriatrics (DGGG), Dr. Alexandra Stolzing

German Society for Immunology (DGfI), Prof. Dr. Frank Emmrich, Dr. Stephan Fricke, Chrsitiane Füldner, Dr. Jens Knauer, Dr. Franziska Lange, Dr. Jörg Lehmann, Christopher Oelkrug, Prof. Dr. Ulrich Sack, Dr. Ulla Schwertassek, Katharina Zoldan

German Society for Cardiology – Cardiovascular Research (DGK), Dr. Alexander Deten

German Society for Parasitology (DGP), Peggy Bodammer

German Society for Regenerative Medicine (GRM), Prof. Dr. Frank Emmrich (member of the scientific advisory council), Dr. Stephan Fricke, Dr. Alexandra Stolzing

German Society for Stem Cell Research (GSZ), Prof. Dr. Frank Emmrich

German Society for Virology (GfV), Dr. Sebastian Ulbert

German Interdisciplinary Association for Intensive Care and Emergency Medical Aid (DIVI), Prof. Dr. Steffen Mitzner

German Morbus Crohn / Colitis Ulcerosa Association DCCV, Peggy Bodammer

German Physiologic Society (DPG), Dr. Alexander Deten

German Sepsis Society (DSG), Prof. Dr. Steffen Mitzner, Martin Sauer

German Society for Clinical Chemistry and Laboratory Medicine (DGKL), Prof. Dr. Frank Emmrich, Prof. Dr. Ulrich Sack

German Zoologic Society (DZG), Gustavo Makert dos Santos

German Ethics Council, Prof. Dr. Frank Emmrich

German Association of University Professors and Lecturers (DHV), Dr. Alexander Deten

European WNV Research Platform, Dr. Sebastian Ulbert

European Autoimmunity Standardization Initiative (EASI), Prof. Dr. Ulrich Sack (executive board)

European Macrophage and Dendritic Cell Society (EMDS), Dr. Claus Kerkhoff

European Molecular Biology Laboratory (EMBL) Alumni Association, Dr. Sebastian Ulbert

European Renal Association – European Dialysis and Transplant Association (ERA-EDTA), Prof. Dr. Steffen Mitzner

European Society for Artificial Organs (ESAO), Prof. Dr. Steffen Mitzner

European Society for Clinical Cell Analysis (ESCCA), Prof. Dr. Ulrich Sack

Förderverein für Medizinische Ausbildung (Friends and supporters of medical training) (FörMA e.V.), Prof. Dr. Frank Emmrich

Friends of Veterinary Medicine Faculty of the University of Leipzig, Dr. Jörg Lehmann

German Chemical Society (GDCh), Dr. Michael Szardenings

Society for Biochemistry and Molecular Biology (GBM), Dr. Claus Kerkhoff, Dr. Michael Szardenings, Prof. Dr. Frank Emmrich

Society for Chemical Engineering and Biotechnology (DECHEMA), Prof. Dr. Frank Emmrich

Society for Nephrology (GfN), Prof. Dr. Steffen Mitzner

Society for Laboratory Animals (GV-SOLAS), Dr. Jörg Lehmann

Association for the Advancement of Immune Diagnostics (GfID), Prof. Dr. Ulrich Sack (executive board)

GLP Commission, Prof. Dr. Ulrich Sack (chief executive manager)

International Society for Heart Research (ISHR), Dr. Alexander Deten

International Union for the Study of Social Insects, Gustavo Makert dos Santos

Leipzig Initiative for Biotechnology, Prof. Dr. Frank Emmrich (chief executive manager)

Leipziger Stiftung für Innovation und Technologietransfer (Leipzig foundation for innovation and technology transfer), Prof. Dr. Frank Emmrich (deputy chairman of the board of trustees)

MEDICA German Society for Interdisciplinary Medicine, Prof. Dr. Frank Emmrich

National Research Platform for Zoonoses, Dr. Sebastian Ulbert

Society for Neuroscience (SfN), Dr. Alexander Kranz, Björn Nitzsche, Dr. Daniel-Christoph Wagner, Vilia Zeisig

The International Dyslexia Association (IDA), Dipl.-Psych. Arndt Wilcke, M.A.

Verein zur Förderung der Gesundheitswirtschaft in der Region Leipzig (Association for the promotion of health management in the Leipzig region), Prof. Dr. Frank Emmrich (chief executive manager)

Verein zur Förderung Regenerativer Medizin (Association for the promotion of regenerative medicine), Prof. Dr. Frank Emmrich

Vereinigung von Förderern und Freunden der Universität Leipzig (Association of supporters and friends of the University of Leipzig), Prof. Dr. Frank Emmrich

Central Committee for Animal Protection, Directorate Leipzig, Dr. Jörg Lehmann

PRIZES

The **TRM award 2012** handed out by the Translational Centre for Regenerative Medicine (TRM) at the University of Leipzig went to Dr. Stephan Fricke from the Immunotherapy unit and Professor G Behre on the topic "Regeneration of normal hematopoesis from leukemic stem cells: MIR-155 inhibition and anti-CD4-antibody therapy"

PUBLICATIONS

JOURNAL ARTICLES

Averill MM, Kerkhoff C, Bornfeldt KE. **S100A8 and S100A9 in cardiovascular biology and disease.** Arterioscler Thromb Vasc Biol. 32 (2012), 2, S. 223-9. doi: 10.1161/ATVBAHA.111.236927.

Bañares R, Nevens F, Larsen FS, Jalan R, Albillos A, Dollinger M, Saliba F, Sauerbruch T, Klammt S, Ockenga J, Pares A, Wendon J, Brünnler T, Kramer L, Mathurin P, Mata MD, Gasbarrini A, Müllhaupt B, Wilmer A, Laleman W, Eefsen M, Sen S, Zipprich A, Tenorio T, Pavesi M, Schmidt HH, Mitzner S, Williams R, Arroyo V. **Extracorporeal albumin dialysis with the molecular adsorbent recirculating system in acute-on-chronic liver failure: The RELIEF trial.** Hepatology. 2012. doi: 10.1002/hep.26185. [Epub ahead of print]

Beer S, Gomez T, Dallinger D, Momber I, Marnay C, Stadler M, Lai J. **An economic analysis of used electric vehicle batteries integrated into commercial building microgrids.** IEEE transactions on smart grid 3 (2012), 1, S.517-525. doi: 10.1109/TSG.2011.2163091.

Boltze J, Kleinschnitz C, Reymann KG, Reiser G, Wagner DC, Kranz A, Michalski D; the meeting contributors. **Neurovascular pathophysiology in cerebral ischemia, dementia and the ageing brain – current trends in basic, translational and clinical research.** Exp Transl Stroke Med. 4 (2012), 1:14. doi: 10.1186/2040-7378-4-14.

Boltze J, Reich DM, Hau S, Reymann KG, Strassburger M, Lobsien D, Wagner DC, Kamprad M, Stahl T. **Assessment of neuroprotective effects of human umbilical cord blood mononuclear cell subpopulations in vitro and in vivo.** Cell Transplant. 21 (2012), 4, S. 723-737. doi: 10.3727/096368911X586783.

Boltze J, Schmidt UR, Reich DM, Kranz A, Reymann KG, Strassburger M, Lobsien D, Wagner DC, Förschler A, Schäbitz WR. **Determination of the therapeutic time window for human umbilical cord blood mononuclear cell transplantation following experimental stroke in rats.** Cell Transplant. 21 (2012), 6, S. 1199-211. doi: 10.3727/096368911X589609.

Burkhardt J, Kirsten H, Holland H, Krupp W, Ligges C, Quente E, Boltze J, Ahnert P, Wilcke A. **Association of rs2069459 in the CDK5 gene with dyslexia in a German cohort.** Psychiatric Genetics. 22 (2012), 6, S. 307-308. doi: 10.1097/YPG.0b013e328353aeae.

Burkhardt J, Kirsten H, Wolfram G, Quente E, Ahnert P. **Differential allelic expression of IL13 and CSF2 genes associated with asthma.** Genetics and molecular biology, 35(2012), 3, S. 567-574. doi: 10.1590/S1415-47572012005000055.

Colley H, McArthur SL, Stolzing A, Scutt A. **Culture on fibrin matrices maintains the colony-forming capacity and osteoblastic differentiation of mesenchymal stem cells.** Biomed Mater. 7 (2012), 4:045015. doi: 10.1088/1748-6041/7/4/045015.

De Filette M, Ulbert S, Diamond M, Sanders NN. **Recent progress in West Nile virus diagnosis and vaccination.** Vet Res.43 (2012), 1, S. 16. doi: 10.1186/1297-9716-43-16.

Engelhardt J, Stadler PF. **Hidden treasures in unspliced EST data.** Theory in Biosciences 131 (2012), 1, S.49-57. doi: 10.1007/s12064-012-0151-6.

Fricke S, Fricke C, Oelkrug C, Blatz R, Schönfelder U, Niederwieser D, Hilger N, Ruhnke M, Rodloff AC. **A real-time PCR for the detection and characterisation of Aspergillus species.** Mycoses. 55 (2012), 5, S. 416-25. doi: 10.1111/j.1439-0507.2011.02161.x.

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Wilcke A, Kirsten H, Brauer J. **LEGASCREEN - A multimodal test for early diagnotic of dyslexia.** 11 th Leipzig Research Festival for Life Sciences, 14.12.2012, Leipzig.

Wilcke A. **Genetics of dyslexia - Introduction, results, and a new research project.** 63rd Annual Conference of the International Dyslexia Association, 24.10.-278.10.2012, Baltimore, USA.

Wilcke A. **LEGASCREEN - Ein Kooerationsprojekt zur Entwicklung eines Frühtests für Legasthenie.** Fraunhofer Netzwerttreffen 2012, 4.-5.12.2012 München.

Zeisig V, Becker G, Großmann U, v. Geymüller T, Nitzsche B, Dreyer A, Kluge M, Plesnila N, Sabri O, Boltze J, Barthel H. **Ermittlung von blutfluß-basierten, schlaganfallspezifischen Hirnkompartimenten mittels [15O]H2O-PET an einem neuen Schlaganfall-modell am Schaf.** Deutsche Gesellschaft für Nuklearmedizin - DGN 2012, 25 - 28 April 2012, Bremen.

Zeisig V, Nitzsche B, Dreyer A, Werner P, Jochimsen T, Großmann U, Boltze J, Hoffmann KT, Sabri O, Barthel O. **Innovative Schlaganfallforschung am Großtier mit Hilfe simultaner PET/MRT-Bildgebung.** 11 th Leipzig Research Festival for Life Sciences, 14.12.2012, Leipzig.

Zoldan K, Möllmer T, Fueldner C, Knauer J, Goerigk D, Fuerll M, Kauffold J, Fischer R, Bergfeld U, Pache S, Lehmann J. **Use of immunologic biomarkers in milk for monitoring the systemic health status in Holstein dairy cows.** European Veterinary Immunology Workshop, 2nd-4th September 2012, Edinburgh, Scotland, UK.

Zoldan K, Möllmer T, Füldner C, Knauer J, S Pache, Lehmann J. **Use of biomarkers in milk for monitoring the systemic health status in Holstein dairy cows.** European Congress of Immunology, 5th-8th September 2012, Glasgow, Scotland, UK. In: Immunology 137 (2012), Supplement 1, S. 677.

Zoldan K, Möllmer T, Schneider P, Frank F, Fischer R, Bergfeld U, Pache S, Lehmann J. **Haptoglobin in der Milch - potentieller Biomarker zur Beurteilung des allgemeinen Gesundheitszustands beim Milchrind.** Vortragstagung der DGfZ und GfT, 12./13. September 2012, Halle/Saale

GRADUATION

Berthold, Jana. **Identification and quantification of periodontitis-relevant germs within the framework of establishing a PCR for the implementation of a lab-on-a-chip system.** Fresenius University of Applied Sciences, Zwickau, Diploma.

Dienelt, Anke. **Investigation into the influence of glucose on the osteogenic differentiation of embryonic stem cells.** University of Leipzig, Dissertation.

Dreyer, Antje. **Detection using magnetic resonance imaging and tracing of migration movements of autologous mesenchymal stem cells following experimentally induced stroke in the sheep.** University of Leipzig, Dissertation.

Giese, Anja Adelina. **Establishment of real-time RT-PCR assays for the investigation of potential immunological biomarkers for the health monitoring of dairy cows.** Biberach University of Applied Sciences, Bachelor.

Heinze, Karolin. **Tests for the identification of serum markers in the serums of allergy sufferers by means of a peptide phage display.** University of Potsdam, Master.

Hoffmann, Friederike. **Application of functionalized nanoparticles for targeted transfection using DNA vaccines.** Beuth University of Applied Sciences Berlin, Bachelor.

Kaniowska, Dorota. **Identification of microRNAs involved in osteoblast differentiation of murine embryonic stem cells.** University of Leipzig, Dissertation.

Kerzhner, Alexandra. **Identification of linear B-cell epitopes in the envelope protein of a new European line of the West Nile Virus.** University of Applied Sciences Jena, Master.

Kranz, Alexander. **Investigation into the therapeutic efficacy of placental, mesenchymal stromal cells in a preclinical stroke model.** University of Leipzig, Dissertation.

List, Nora. **Testing of AFP as an alternative freezing medium for the cryopreservation of rat MSC.** Anhalt University of Applied Sciences, Bachelor.

Majunke, Salome. **Investigations into bead-based DNA purification as part of the development of a lab-on-a-chip system for the rapid detection of sepsis pathogens.** Anhalt University of Applied Sciences, Köthen, Master.

Nitzsche, Björn. **Pathomorphological characterization of focal cerebral ischemia and therapeutic effects by means of autologous bone marrow transplantation in the sheep model.** University of Leipzig, Dissertation.

Rasser, Judith. **Characterization of isothermal amplification methods for application in a diagnostic test strip system.** University of Applied Sciences Mittweida, Bachelor.

Riemschneider, Sina. **Effect of benzo[a]pyrene on the activation mechanisms of murine macrophages.** Martin Luther University Halle-Wittenberg, Master.

Schulze, Felix. **Differentiated macrophage activation under the influence of corn oil and benzo[a]pyrenes in infections with salmonella enterica in the mouse.** Lausitz University of Applied Sciences, Bachelor.

Seidel, André. **Immunophenotyping of the infiltrating leukocytes in the stroke region in an experimental stroke model in the rat.** Zittau / Görlitz University of Applied Sciences, Bachelor.

Taubert, Julian. **Therapeutic influence of the transplantation of syngeneic, regenerative cells from fat tissue following experimental ischemic stroke in spontaneously hypertensive rats.** University of Leipzig, Dissertation.

Vemula, Venukumar. **Comparison of affinity tags for the heterologous production of viral proteins used to detect porcine reproductive and respiratory syndrome virus by enzyme linked immunosorbent assay.** Martin Luther University Halle-Wittenberg, Master.

von Geymüller, Teresa. **Influence of an autologous bone marrow cell therapy on reactive astrogliosis and glucose transporter 1 expression in grey and white matter of the cerebrum following focal cerebral ischemia in the sheep.** University of Leipzig, Dissertation.

PATENTS

The patent portfolio of the Fraunhofer IZI currently holds 20 patent families (two having been granted and seven new applications) which are available for use in cooperation projects as well as for direct commercialization and licensing.

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FURTHERANCE

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

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The Fraunhofer IZI would like to thank the European Union, the Federal Ministry for 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 for Education and Research and the Free State of Saxony. In the same manner, the expenses of about 11 million Euros for construction and equipment of the extension building were covered. The plot of land is provided by the City of Leipzig in hereditary leasehold and free of charge.

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

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DIE FRAUNHOFER-GESELLSCHAFT IN PROFILE

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

At present, the Fraunhofer-Gesellschaft maintains 66 institutes and independent research units. The majority of the more than 22,000 staff are qualified scientists and engineers, who work with an annual research budget of 1.9 billion euros. Of this sum, more than 1.6 billion euros is generated through contract research. More than 70 percent of the Fraunhofer-Gesellschaft's contract research revenue is derived from contracts with industry and from publicly financed research projects. Almost 30 percent is contributed by the German federal and Länder governments in the form of base funding, enabling the institutes to work ahead on solutions to problems that will not become acutely relevant to industry and society until five or ten years from now.

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

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

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

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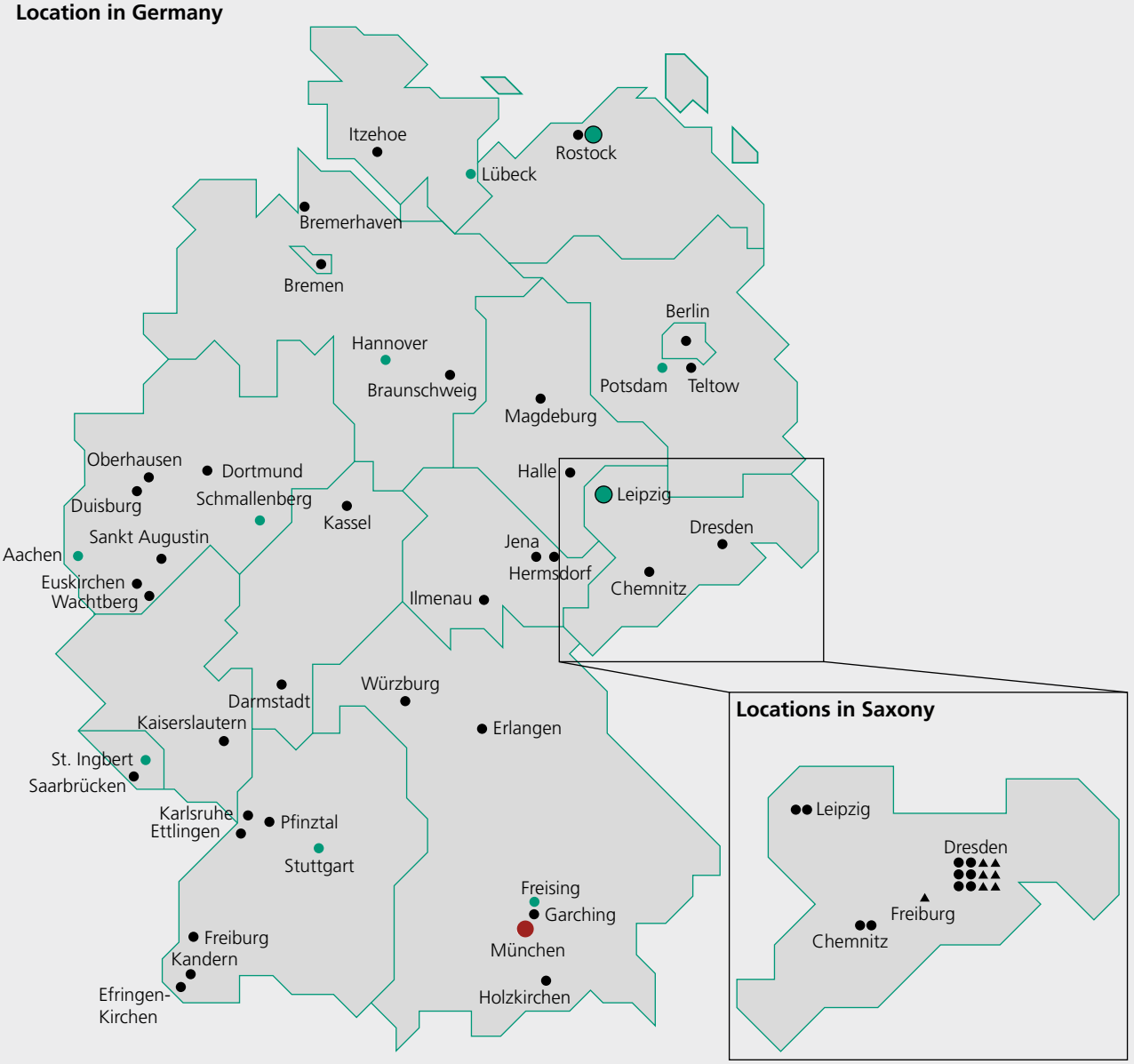

- Fraunhofer Institute
- Central office of the Fraunhofer-Gesellschaft, Munich
- Location of institute of the Fraunhofer Group for Life Sciences
- Fraunhofer IZI

- Institute / independent research establishment
- Other location

FRAUNHOFER GROUP FOR LIFE SCIENCES

Zur Stärkung der Biowissenschaften, Biomedizin und Biotechnologie wurde im Jahr 2001 der Fraunhofer-Verbund Life Sciences (VLS) gründet. Er umfasst derzeit sechs Institute.

In terms of expanding research revenue as well as business spin-offs, the Fraunhofer Group for Life Sciences is one of the Fraunhofer-Gesellschaft's most dynamic areas of research.

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- Medical translational research and biomedical technology: The challenge of innovative diagnostics and personalized therapy
- Regenerative medicine: The challenge of qualified biobanking and controlled self-healing
- Healthy foods: The challenge of high consumer acceptance and disease prevention
- The new potential of biotechnology: The challenge to learn from nature for industrial exploitation
- Process, chemical, and herbicide safety: The challenge of environmental and consumer protection

The elected spokesman of the Fraunhofer Group for Life Sciences is Prof. Dr. Thomas Hirth, who heads the Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB in Stuttgart. Since 2008, Prof. Dr. Frank Emmrich (head of the Fraunhofer IZI) is deputy spokesman.

Institutes of the Fraunhofer VLS

- Fraunhofer Institute for Biomedical Engineering IBMT
- Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB
- Fraunhofer Institute for Molecular Biology and Applied Ecology IME
- Fraunhofer Institute for Toxicology and Experimental Medicine ITEM
- Fraunhofer Institute for Cell Therapy and Immunology IZI
- Fraunhofer Institute for Process Engineering and Packaging IVV
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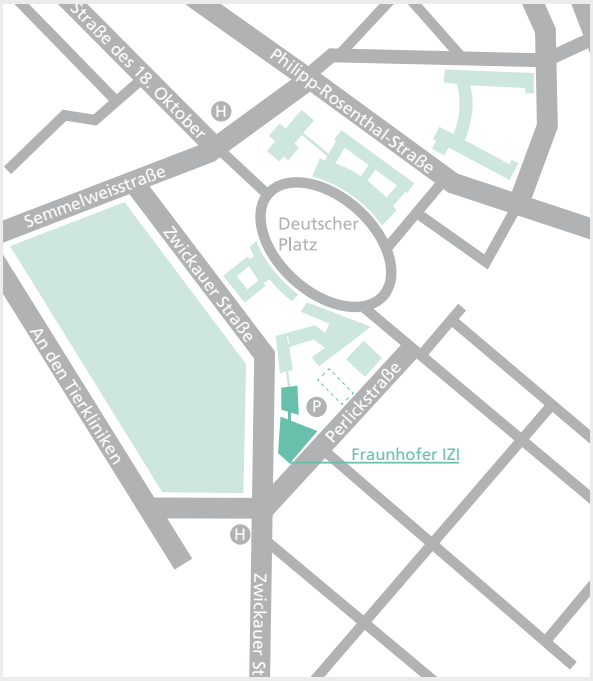

By car

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

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

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

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

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Layout & typesetting
Michaela Grahn

Translation
LSI World of Languages GmbH

Photo acknowledgements
except as noted otherwise all pictures and figures
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Printed by
FISCHER druck&medien, Großpösna near Leipzig

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