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FRAUNHOFER INSTITUTE FOR CELL THERAPY AND IMMUNOLOGY IZI

ANNUAL REPORT 2011

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2011

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PREFACE

PROF. DR. FRANK EMMRICH

IN CONVERSATION WITH THE DIRECTOR

For you as Institute Director, which results were the most impressive in the 2011 business year? At the start of the year, work began on the Fraunhofer Future Foundation project "Ribolution". Coordinated by Professor Friedemann Horn from the Fraunhofer IZI, a total of five Fraunhofer Institutes (IGB, FIT, ITEM, IPA) are working together with clinical partners who are highly esteemed on an international level to identify new types of biomarker for the diagnosis and follow-up of rheumatoid arthritis, chronic obstructive pulmonary diseases and prostate cancer. Beyond the characterization of biomarkers, extremely miniaturized technological platforms are also being developed as part of this project in order to make the search for markers significantly more cost-effective. These biomarkers are so-called "non-coding RNAs", which will help facilitate insights into the working of cells. In March 2011, we marked the founding of the project group Extracorporeal Immunomodulation (EXIM) by holding a scientific symposium together with the Minister of Science of the State of Mecklenburg-Vorpommern and the Vice Chancellor of the University of Rostock. At the beginning of the year, the Fraunhofer IZI also managed to acquire the Fraunhofer-Gesellschaft's largest new client project in the quarter. Due to our competencies in the area of cell engineering manufacturing processes – which have now come to be recognized on an international level – an American consortium of companies has commissioned us to develop a dendritic cell vaccine for the treatment of malignant brain disease. This prompted a subsidiary company to be founded in Leipzig. In a consortium headed by the Fraunhofer Institute in Saxony (FEP Dresden), the Fraunhofer IZI won the extremely positively assessed project "SteriHealth" in the "Future Markets" call for tenders. This project will develop new ways of killing germs in clinical facilities. At the end of the year we were able to achieve a further success in cooperation with the Max Planck Institute for Human Cognitive and Brain Sciences in Leipzig. One of the highly esteemed Max Planck / Fraunhofer research groups will now be set up in Leipzig. Under the motto "Legascreen", the group will look at speech development in young children and genetic diagnostics of poor reading and spelling (dyslexia). The aim here is to develop a testing procedure to diagnose dyslexia at an early stage.

February 2011 saw the topping out ceremony for the first extension building. The extension will be completed in 2012. How important is this extension for the institute and what is planned for the future? The extension building became necessary because an entire spectrum of laboratory capacities was no longer enough to cater for the hugely increased number of employees (currently 195) and projects (over 100) due to the institute's extremely dynamic growth. There was a particular lack of space for clean rooms where cell technology can be developed under the highest pharmaceutical standards. Much to our regret, we were unable to handle a large number of contract offers worth several million euros due to a lack of capacity. This bottleneck will hopefully have subsided as of mid-2012 when the extension is put into operation. However, there are already signs that this extension will soon also no longer be sufficient. Over the coming decades we expect an increasing automation of cell-oriented analysis and processing methods.

This requires the appropriate workshops and laboratory and assembly units. Increasingly intensified collaboration with Fraunhofer Institutes and external partners in the field of engineering will also be tied in with this. The many Fraunhofer Institutes in Dresden lend themselves particularly well as partners in this respect. The State Government and Fraunhofer-Gesellschaft are giving off extremely positive signals in terms of backing further extension buildings on the Fraunhofer IZI.

Last year, the Fraunhofer IZI organized the "World Conference on Regenerative Medicine" in Leipzig, together with the Translational Centre for Regenerative Medicine (University of Leipzig). How has this event developed over the past few years and what does it mean to you? The "World Conference on Regenerative Medicine" takes place every two years at the Congress Center Leipzig on the trade fair grounds and has continuously gained in appeal. In 2011, around 1 000 attendees took part in the conference, which included almost 400 scientific papers and 65 company presentations. The event was opened with a talk held by Senator Art Torres (ret.), Vice President of the "California Institute for Regenerative Medicine" (CIRM). With three billion US dollars, the CIRM is the financially strongest research organization for regenerative medicine in the world. Together with the University of Leipzig, our scientists are participating in a close cooperation funded by the Federal Ministry of Education and Research. As Conference President, I was particularly pleased with the distinct increase in the scientific quality of the papers. One colleague, a renowned British researcher, said he thought the Leipzig conference was the most important event in the field throughout Europe.

Last year you attended various debates as member of the German Ethics Council. Which topic areas struck you as being particularly significant and how will they change our lives over the course of years to come? The German Ethics Council's position paper on preimplantation genetic diagnosis (PGD) was certainly the most intensely discussed topic in public. As was the case a short while later in the German Bundestag, the majority of German Ethics Council members voted for the controlled introduction of PGD in Germany. If you followed the press reports at the beginning of 2012 on the first PGD baby in Germany and you read about the suffering previously endured by the family from Lübeck, you most likely formed the opinion that the right decision had been made here. Without submitting a public statement, we at the Ethics Council did of course discuss the judgement of the European Court of Justice, which ruled that products made from or using embryonic stem cells cannot be patented in Europe. The consequences this decision will have on international cooperation on a scientific and economic level remain to be seen. At present, the German Ethics Council, as part of a special working group, is addressing regulatory approaches and their ethical derivation which will further develop the German Genetic Diagnostics Act (Gendiagnostikgesetz) and also involve research in the area of genetic diagnostics. Besides this, the German Ethics Council has also been involved in extremely intense discussions on the topic of "biobanks", particularly taking into account rights to privacy of cell and tissue donors, the obligation for transparency and disclosure, as well as the control framework for biobanks.

Which objectives are you and the institute set to tackle next year? Signs are already emerging that 2012 will be the Fraunhofer IZI's most successful year. In the first couple of months we were already able to contractually bind orders and projects in the value of over ten million euros for 2012, meaning that our institute is able to research and work on a secure basis. We are also becoming increasingly more recognized on an international scale, with our largest development contracts now coming from outside Europe. As an international research partner of the Chonnam National University in South Korea, we have managed to obtain funding in the ambitious research competition held by the Korean "National Research Fund". In doing this, we were able to contend with 20 Korean universities in a competition which has a general success rate of only 10 percent. We will expand these and other contacts over the coming year and strengthen our international relations through a whole series of conferences which we are helping to organise. This includes the "7th International Symposium on Neuroprotection and Neurorepair" which is being held in Potsdam in May, and the "Fraunhofer Life Sciences Symposium" together with the "7th Annual Congress of the German Society for Stem Cell Research" in Leipzig. Over the past few years, in connection with large research projects, the Fraunhofer IZI has contributed to the founding of companies in Leipzig on several occasions. In 2012, we are also expecting at least two spin-off companies to be founded. By working closely with experts at the University of Leipzig who are proficient in dealing with spin-offs, we will continue to strengthen the location. On this point, I would like to pay special thanks to our colleagues, and also our partners and clients, for their commitment and support. We are looking forward to working together in the coming year.

HIGHLIGHTS 2011

THE PATH TO EUROPE RUNS THROUGH SAXONY

With research and development services in and around the field of cell therapy, the Fraunhofer Institute for Cell Therapy and Immunology quickly managed to acquire two major projects this year with international partners and clients. With both these and other projects, the Fraunhofer IZI was able to demonstrate that it is well established with respect to international competition. With the extended clean room capacities in the new extension building, which will be available as of 2012, the institute is optimally equipped for further major contracts.

The assignment placed by an American biotechnology company got the ball rolling. Northwest Biotherapeutics, Inc. is developing an innovative therapeutic procedure for the treatment of glioblastomas. In order to also tap the European market with this procedure, Northwest Biotherapeutics has commissioned the Fraunhofer IZI with technology transfer. The institute's initial task is to establish appropriate processes in its clean room facilities and to obtain the associated regulatory authorization. Further down the line, the first clinical investigational drugs are also to be manufactured at the Fraunhofer IZI.

At present, glioblastomas can only be treated to a limited extent and without a satisfactory level of success. The treatment options are limited to surgical procedures, radiotherapy and chemotherapy, which are all associated with significant risks and side effects: once a brain tumor is diagnosed, patients have an average of 14 months left to live. With the autologous immunotherapy DCVax® Brain, it is hoped that significantly better treatment successes, a higher chance of survival and fewer side effects will be achieved.

The autologous immunotherapy DCVax® Brain is based on dendritic cells. These cells play a central role in regulating the immune system. As tumor tissue evolves from the body's own cells, it is often not recognized by the immune system as being foreign and is therefore not attacked. Through the DCVax® procedure, the dendritic cells are educated to recognize certain tumor antigens (biomarkers) which are particular features of glioblastoma tumor cells. The modified cells subsequently stimulate T cells, B cells and antibodies as well as further mechanisms of the immune system to combat the respective tumor cells.

The Australian company Prima Biomed Ltd. has already been substantially supported by the Fraunhofer IZI in founding a German affiliate. The company is developing an innovative therapeutic procedure for treating ovarian carcinoma. Before the procedure can also be made available to European patients, another clinical trial (phase IIa) is required to verify safety and efficacy. This trial forms part of the joint cooperation project, which will be funded by a total volume of 4.1 million euros using funds from the European Regional Development Fund (ERDF) via the Sächsische Aufbaubank (Saxon Development Bank). On 8 August 2011, State Minister Professor Sabine von Schorlemer personally announced that funding had been approved. The State Minister for Science and the Arts also took the opportunity to visit the Fraunhofer IZI's GMP facility where the investigational drugs will be manufactured for clinical trial as of the start of 2012.

The autologous immunotherapy CVac™ is also based on the modification of dendritic cells. The CVac™ process modifies the patient's immunocompetent cells in such a way that they are able to recognize tumor cells and activate different defence mechanisms in the immune system. In doing this, dendritic cells are educated to recognize a certain protein (biomarker) which only exists on ovarian carcinoma tumor cells. The immune system is thus in a position to specifically attack the tumor cells without impairing healthy cells. As a result, this form of treatment is significantly gentler for patients than radiotherapy or chemotherapy, and it also promises lower relapse rates.


WORLD CONFERENCE ON REGENERATIVE MEDICINE

Since 2007, the Fraunhofer IZI has organized both the biennial "World Conference on Regenerative Medicine" in Leipzig, and the annual "Fraunhofer Life Science Symposium".

In 2011, almost 1 000 top international experts from the fields of research, clinical medicine, economy and politics accepted the invitation to Leipzig to discuss the newest findings in regenerative medicine. Between 2nd and 4th November 2011, scientists from over 40 nations presented their research work in the areas of stem cell research, cell therapy, tissue engineering, biomaterials and molecular bases, in the form of 190 talks and 260 poster presentations. Over 70 sponsors and exhibitors, 13 media partners and 17 supporting professional societies attest the increasing interest in the interdisciplinary thematic conference. As guest of honour on the opening evening, Senator Art Torres from the California Institute for Regenerative Medicine (CIRM) spoke to attendees about the extensive activities of the US State of California, one of the global hotspots in the field of regenerative medicine.

This year, particular attention was paid to contributions on so-called induced pluripotent stem cells (iPS cells). These cells promise to be an alternative to the ethically disputed use of embryonic stem cells. Beyond this, the extraction and therapeutic application of differentiated stem cells was also discussed. Professor Michele De Luca, University of Modena (Italy), spoke about the successful application of patients' own stem cells in cases of chemical injuries to the cornea.

On the topic of tissue engineering, Professor Laura Niklason, Yale School of Engineering and Applied Science in New Haven (USA), gave insights into the manufacture of lung tissue for transplants. Her approach targets the creation of acellular lung scaffolds which are populated with the recipient's own cells.

Last but not least, the regulatory conditions for the transfer of therapeutic approaches to clinical practice were discussed alongside ethical issues.

The International Veterinarian Regenerative Medicine Society (IVRMS) successfully organized various sessions for the second time, which highlighted veterinary medical aspects of regenerative medicine. Veterinary medical topics are also of huge interest to human medicine as the results of treating large animals, in particular, supplies human medicine with valuable pre-clinical data.

The PhD sessions, which were offered for the first time, received a surprisingly good response. In special sessions, PhD students as well as young scientists had the opportunity to present their research work to an international audience, moderated by experienced and renowned scientists.

FRAUNHOFER IZI SETS UP PROJECT GROUP IN ROSTOCK

For several years now, numerous close alliances have existed with the University of Rostock, as well as the desire to install a Fraunhofer IZI project group in Rostock. On March 14, the efforts of all those involved came to fruition and the group "Extracorporeal Immunomodulation" was established.

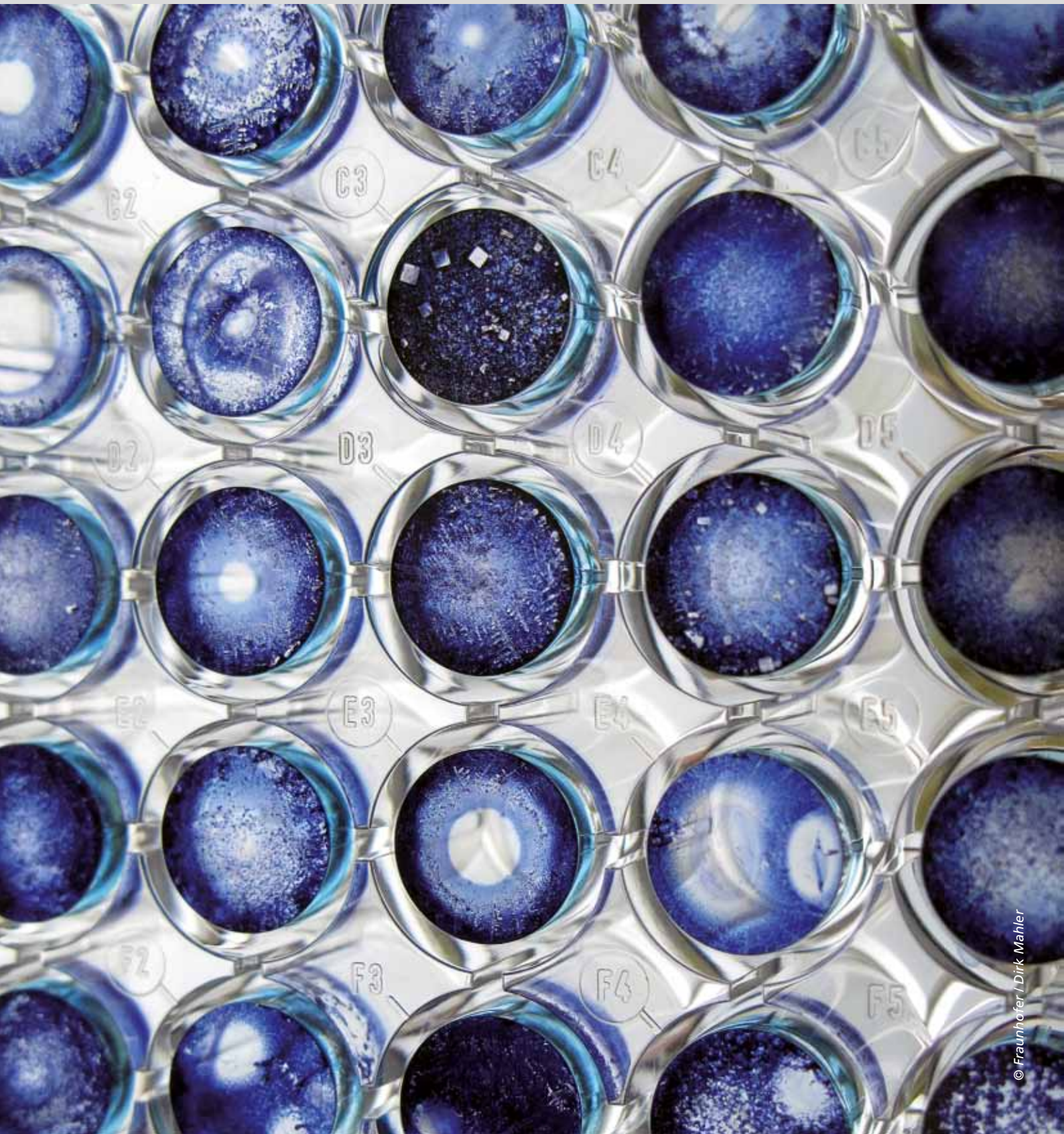
Equipped with over 5.5 million euros worth of funding from the EU and the Federal State of Mecklenburg-Vorpommern, the group took up work at the Fraunhofer IZI under the direction of Professor Steffen Mitzner. The group pursues three core areas of research and development: 1.) developing and testing immunomodulating therapies; 2.) developing and applying model systems of the human digestive system; and 3.) operating a clinical study site.

Developing new treatment approaches based on classic extracorporeal technology platforms such as dialysis and plasma separation falls within the area of developing and testing immunomodulating therapies. There is particular emphasis on the development of extracorporeal blood treatment processes for septicaemia. As part of this, failed and impaired immune system functions are replaced in stages. The process first effectively removes noxious substances such as bacterial toxins and stimulates the immune system.

In developing model systems, the focus lies on models of the intestinal wall, stomach or pancreas. With the aid of this, bacterial infections, food allergies, food additives and potentially toxic substances are to be examined and appropriate therapeutic strategies are to be developed. A clinical study site aims to quickly transfer the project group's scientific concepts into clinical applications. The study site is to plan, prepare, conduct and evaluate clinical trials in close cooperation with clinical units in the region.

Supported by the Fraunhofer IZI, an appointments committee at the University of Rostock has appointed Professor Mitzner to be W3 Professor and has also assigned him clinical responsibility.

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 research, 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 15 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 "Press and Public Affairs" and "Business Development and Patent Management".

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.

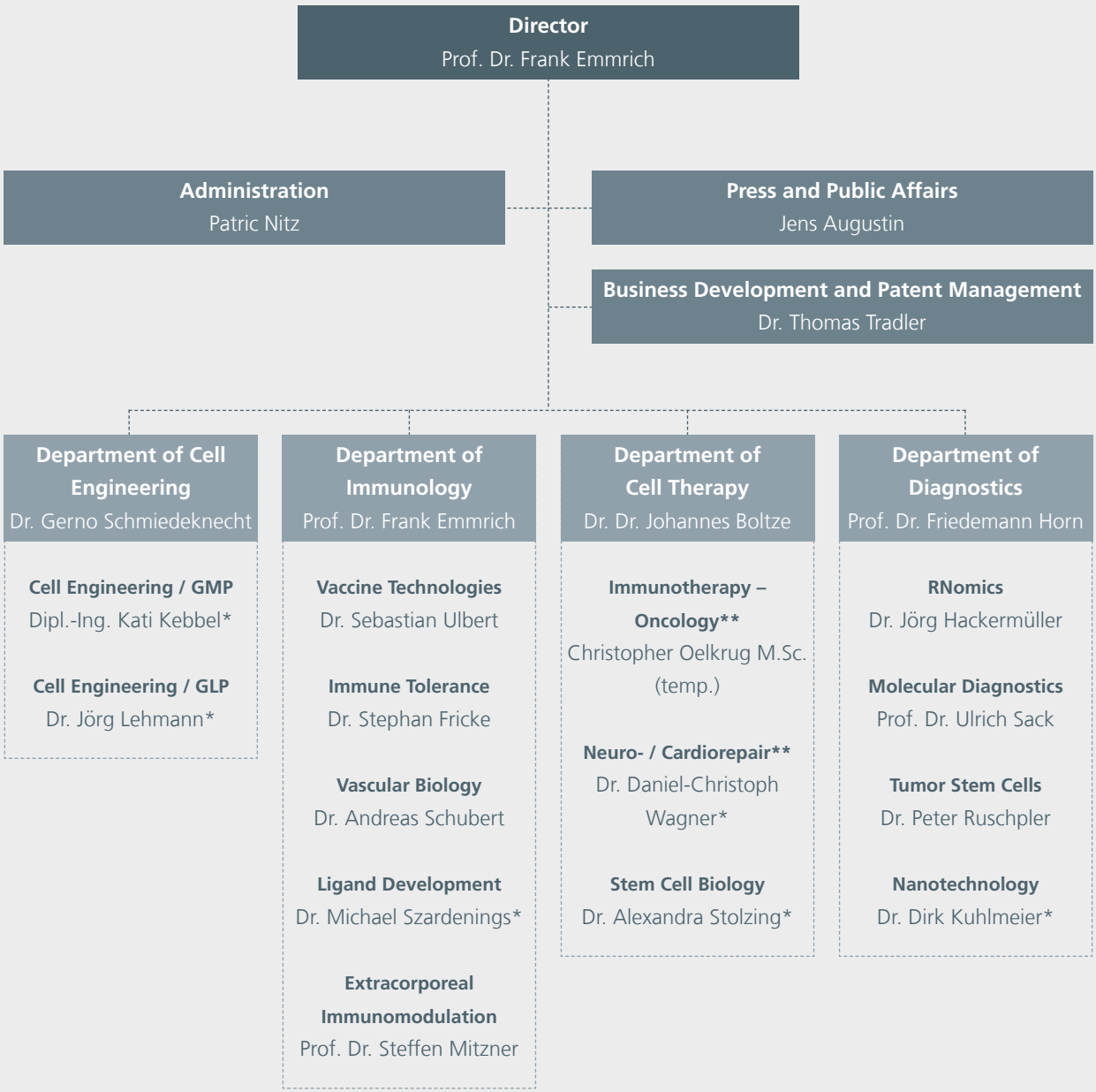
The institute is particularly proud of the ability to offer its clients a varied and wide range of services within the fields of drugs, cell therapy, diagnostics and biobanks. The executive department "Business Development / Patent Management" sees itself as a central point of reference in terms of communicating 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. (The challenge for 2012 will be to also translate this optimum into the extension work.) 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.

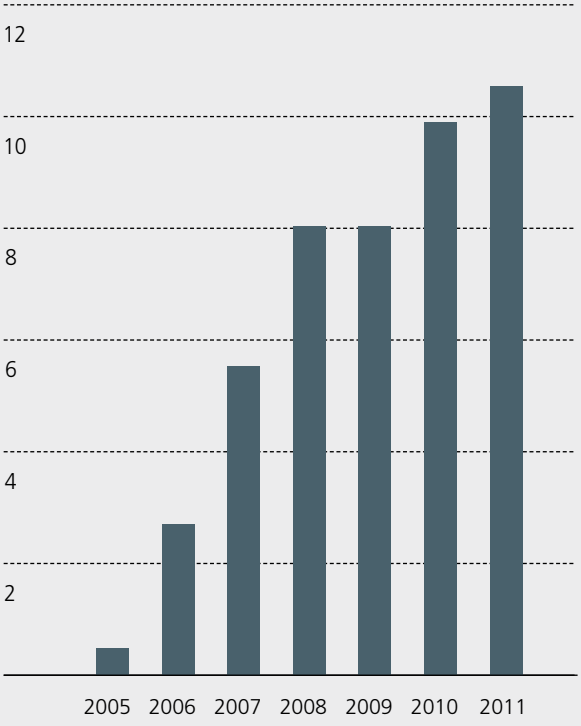


* Deputy head of department.
** Headed by Dr. Dr. Johannes Boltze in the reported year.

THE INSTITUTE IN NUMBERS

Financial volume

Mio €

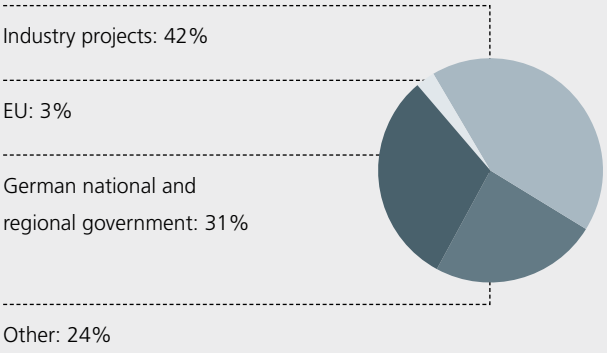


Overview of the projects

	number 2011	volume 2011
German national and regional government	22	4 054 728 €
EU	2	262 199 €
Industry projects	30	2 222 780 €
Other	17	1 323 136 €
Total	**71**	**7 862 843 €**

Overview of the projects

Number of projects



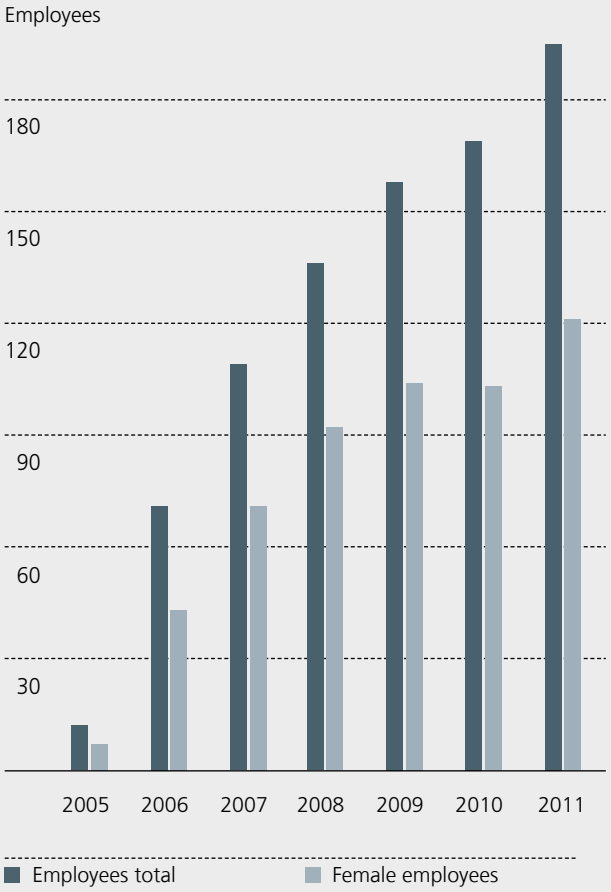
Budget

The budget (turnover and carryover) was increased to over 10 million euros in 2011. Due to the optimized cost structure and the fact that the majority of projects were handled within budget, a positive carryover was generated in the year under review. This chiefly serves to secure the uncertainties of the extension work, as the one-off start-up costs and ongoing maintenance costs could not be calculated precisely due to the work's technical complexity. The extension building is planned to go into operation in summer 2012.

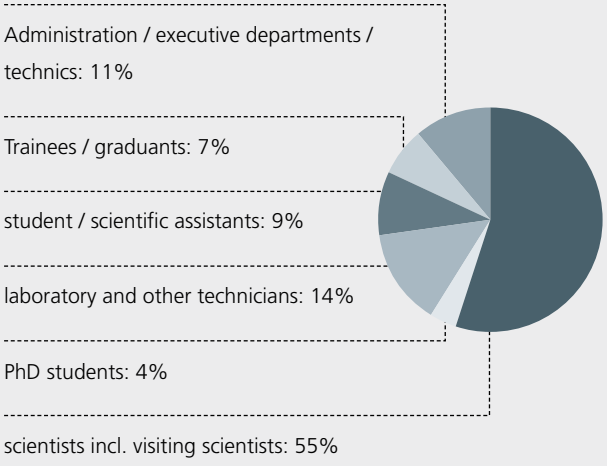
Projects

At the turn of the year into 2012, 71 projects were being handled. In all, the volume of individual projects has increased. This is particularly notable when considering industry projects. Besides a decrease from 35 to 30 projects, an increase in project volume amounting to 430 000 euros was also achieved. Among others, this is the result of successfully acquiring contracts for large projects.

Employees



Workforce composition



Human resources

A steady growth in personnel is also connected to the growth in budget. Therefore, in the 2011 reporting year, the entirety of those involved in the success of the Institute increased by 26 to a total of 195 people. Further important aims of the institute regarding human resources development also follow this trend. For example, a higher-than-average employment ratio of women at a level of 62 percent was, in turn, achieved. Moreover, the ratio of specialist scientific staff, including guest researchers working at the institute, was increased by five percentage points to 55 percent. Alongside research and project management duties, their role also invariably includes supervising junior research staff, whose employment rate has increased to 14 percent. By linking scientific excellence with above-average motivation and efficiently structuring work, the institute is very well positioned when it comes to competing on an international level.

DEPARTMENT OF CELL ENGINEERING

IN CONVERSATION WITH DR. GERNO SCHMIEDEKNECHT

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Of all the projects the department handled in 2011, which are you particularly proud of? I am particularly proud of a project with the American companies Cognate BioServices Inc. / Northwest Biotherapeutics Inc., which we are supporting during the preparatory and conduct stages of a clinical trial for the treatment of brain tumors. As part of the project, the complex manufacturing process for the autologous immunotherapeutic DCVax® L-Drug (Brain), based on dendritic cells, will be transferred to Europe and adapted to European legal foundations, and a manufacturing authorization in accordance with Section 13 of the German Drug Act (AMG) will be obtained. A clinical trial planned in Germany is to subsequently be provided with the individual investigational medicinal products. This project was the largest industry project for a new client undertaken within the Fraunhofer-Gesellschaft in the first quarter of 2011. A significant achievement that I am also very proud of is the successful completion of a GLP inspection. Within the scope of this inspection, foundations were laid for the GLP-compliant conduct of preclinical drug tests for advanced therapy medicinal products (ATMP) in small and large animal models. The Cell Engineering / GLP Unit has assumed a leading role in this field.

What were the greatest challenges for the department in 2011 and how would you describe the outlook for the coming year? The complexity and novelty of drug candidates does not only pose an enormous challenge for our staff, but also for the authorities and clients; with these challenges, all those involved are constantly developing their knowledge and having to solve complicated issues on a daily basis. Adhering to the time schedules provided by project partners presented us with a number of challenges due to complexity and novelty, and was, admittedly, not always easily feasible. What we want to do in 2012 is to move projects which are close to the clinical use, such as those with Prima BioMed Ltd. or Cognate BioServices Inc. / Northwest Therapeutics Inc., into the clinical phase. Details which have become publicly known about these projects have already raised hopes among patients this year; such expectations have, however, not yet been met due to long-winded preparatory work necessary to meet all of the legal standards. Once the clinical trials begin, we hope to be able to help some of those affected through their trial participation.

The Institute's first extension building will open in 2012. To what extent is this addition to the infrastructure important for the Department of Cell Engineering? The existing GMP facility in the Department of Cell Engineering is being used to its full capacity, which sadly means that we are currently unable to handle new projects. By way of contrast, there is a high number of potential project partners with whom new exciting cell therapy projects can finally be realized thanks to the extension building.

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 meet strict legal guidelines (such as GMP, GLP, etc.) in such a way that a safe application is possible during preclinical and clinical trials. At the Institute, this is done by obtaining manufacturing authorizations in accordance with Section 13 of the German Drug Act (AMG) or GLP certificates, which partly represents one entire year's work or more for each individual project.

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
- 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 54.

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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, cancer vaccines). Here, the whole range from process development and validation to the manufacture of investigational medicinal products is covered.

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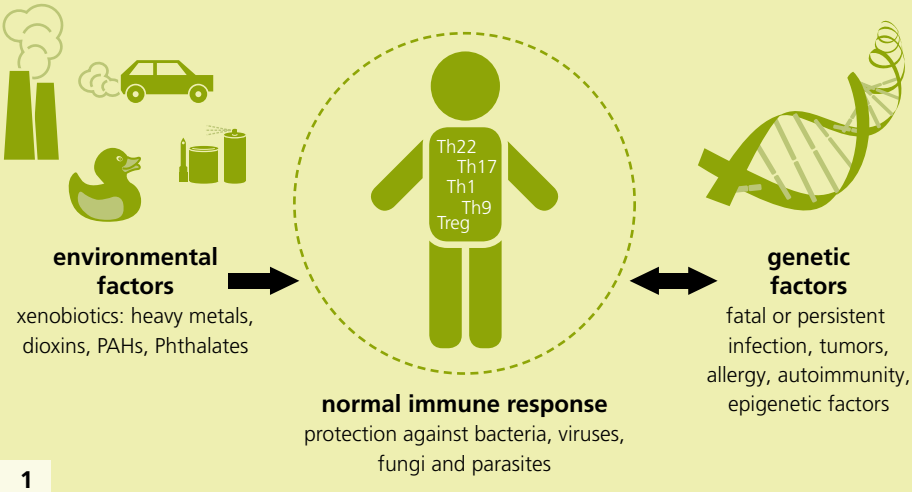
Cell Engineering / GLP Unit

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.



1

PROJECTS

Models for analysing harmful substances and their impact on the immune system

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Every day, we are exposed to foreign substances which are partly considered as being problematic (e. g. softeners in car parts, heavy metals from tyre wear, softening agents in household objects, PAHs in plastic products, exhaust fumes, and overly roasted food products). Although the effects of various harmful substances can already be artificially represented in vitro, complex animal models are indispensable for the examination of a potential immunomodulatory capacity in vivo; until now, however, such models have rarely been available. There is still a lack of standardized in vivo methods to demonstrate the immunotoxicity of poisonous substances. Many tests are carried out without activating the immune system, i. e. without antigen contact, and therefore only yield incomplete results. The actual effect of harmful substances on the immune system is not assessable until it has been investigated in combination with antigen contact. Relevant activation of the immune system by an infection is depicted as the best indicator model for immunotoxicology.

With the aid of the murine salmonella infection model developed in our unit, the influence of harmful substances, such as phthalates and BaP, on the immune system during a model infection is to be examined as part of this project. In the medium term, this in vivo model could also be used for the immunotoxicology testing of other xenobiotics or drugs.

The effect of such foreign and harmful substances is often not directly on the immune system, but rather via specific receptors (e. g. AhR). It therefore tends to be difficult to directly ascertain changes in the subtoxic range. The Salmonella enterica infection model we developed in the mouse is very well characterized in terms of immune response and, as an in vivo model, also allows the measurement of indirect effects on the immune system. With reference to its infection dose and the resulting experimental parameters (e. g. survival, germ load in different organs, specific cytokine responses), the model is set up in such a way that even small changes in the immune status of laboratory animals lead to dramatic changes in individual parameters. Thereby, even minimal changes in the immune status of laboratory animals can be detected, which are triggered by exogenously applied and potentially immunomodulatory substances.

1 *Overview: Influence of xenobiotics on the immune system.*

1

2

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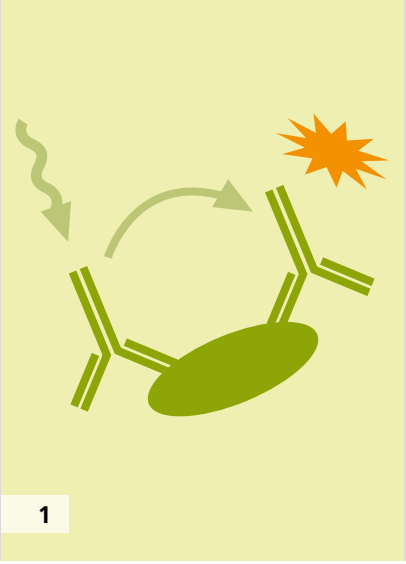
Process transfer and manufacture of the immunotherapeutic DCVax® L-Drug (Brain)

The American biotechnology company Northwest Biotherapeutics Inc. is planning to conduct a phase II clinical trial to examine the efficacy of their immunotherapeutic DCVax® L-Drug (Brain). DCVax® L-Drug (Brain) is an advanced therapy medicinal product based on autologous dendritic cells to treat glioblastomas, which has already been utilized in initial clinical trials in the USA. As part of the project, the existing GMP manufacturing process, including quality controls, is first to be transferred to Leipzig by the American company Cognate BioServices Inc., where it is also to be adapted in line with European legal foundations. The aim is for the responsible pharmaceutical supervisory authority to issue manufacturing authorization specifically for DCVax® in accordance with Section 13 of the German Drug Act (AMG). After obtaining manufacturing authorization, the focus will move to manufacturing, quality control and providing the clinical investigational drugs.

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 is process validation, which includes the fully documented manufacturing and quality control of three validation batches. Besides process validation, analytical methods will also be validated. 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. Furthermore, it is necessary that leukapheresis procurement facilities and neurosurgical tumor procurement centres are qualified to guarantee high-quality procurement and testing of patients' autogenous base materials.

The application for manufacturing authorization in accordance with Section 13 of the German Drug Act (AMG), which has been submitted to the responsible pharmaceutical supervisory authorities (Landesdirektion Sachsen, Paul-Ehrlich-Institute), is currently in the review phase. After reviewing the application documents and once the manufacturing process and analytical methods have been fully validated, a GMP acceptance inspection will then take place. If this inspection is successful, the requested manufacturing authorization will be granted. This official authorization then forms the precondition for providing the cell-based investigational medicinal products for the planned clinical trial.

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



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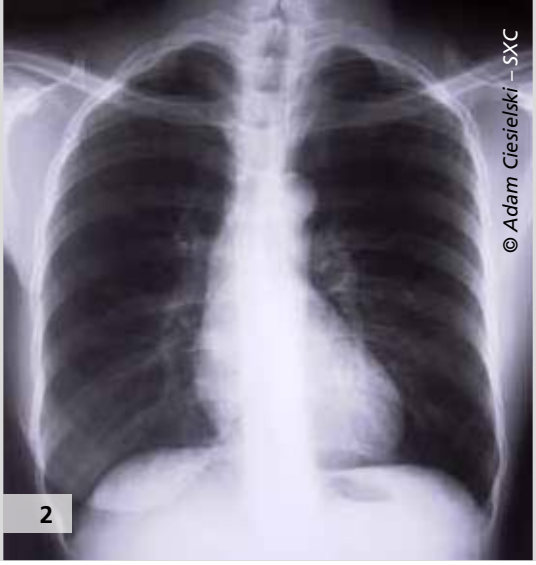

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2

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 could be 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 current joint project is to detect VEGF as a biomarker for the early diagnosis of bronchial carcinoma using an innovative device system within the framework of point-of-care diagnostics.

As part of the preliminary work for this project, the concentration of VEGF165 in patients' exhaled breath condensate has been identified as a promising biomarker candidate for the differential diagnosis of bronchial carcinoma. So far, however, the extent to which these biomarkers permit a sufficiently early detection of this malignant neoplasia in routine use, and therefore significantly improve the individual chances of being cured, is vague.

The project is being conducted as a close collaboration between the Fraunhofer IZI, the Institute for Clinical Immunology of the Faculty of Medicine at the University of Leipzig, Compart Umwelttechnik GmbH in Weissenfels and GESA Automation GmbH in Teuchern. Besides VEGF165, there are also other tumor markers or biomarkers for the early diagnosis of autoimmune diseases or of Alzheimer's disease which can be regarded as diagnostically interesting protein biomarkers that may be detectable by a device platform to be developed in the course of the research and development project. By adapting the sampling modules of the device platform at a later stage, these protein biomarkers can 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. 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. We aim to tackle this challenge within the framework of this project.

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1 *Immunochemical detection procedure in line with the FRET or PRET procedure.*

2 *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.*

DEPARTMENT OF IMMUNOLOGY

IN CONVERSATION WITH PROF. DR. FRANK EMMRICH

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You have been handling a large EU project since February 2011. What does this mean for the institute? Under the coordinating leadership of Dr Ulbert from our department, nine international research units are working on the development of a new type of vaccine against the West Nile Virus (WNV). We are particularly pleased to note the involvement of an extremely reputable unit from the USA. Using the example of the USA, it was able to be observed over the past few years how quickly the virus spread throughout the entire North American animal kingdom, unfortunately also infecting many humans, with the number of human deaths surpassing 1 000. In this respect we are conscious of the responsibility to protect EU citizens from WNV infection waves, which have already been detected in rudimentary stages in south east European countries. Preventing and combating infectious diseases requires cross-border communication and cooperation. For this purpose, in 2011, all of the large collaborative projects funded by the European Union on the development of virus vaccines joined forces to collectively share and exchange knowledge. We are very happy and also rather proud to also be able to make significant contributions in this regard.

What particular successes could the Department of Immunology record last year? We are pleased with the two appointments made within the department. Dr Hans-Peter Deigner was appointed to professor of pharmacology at the University of Furtwangen. Professor Steffen Mitzner was appointed to W3 professor at the University of Rostock. In this capacity he also bears immediate clinical and medical responsibility at Rostock University Hospital. We are a member of a research consortium made up of six Fraunhofer Institutes in the Fraunhofer "Future Markets" initiative. With the "SteriHealth" project we have jointly been awarded a contract to develop a new type of germ-killing sterilization process for medical facilities. Furthermore, we have decisively enhanced a new treatment procedure to increase resistance to parasite infestation in poultry farming. This resulted in a significant follow-up contract from one of the most internationally prominent poultry farming companies in Europe. A license agreement was concluded with a Leipzig company on a testing procedure which we developed. This procedure allows a major virus disease in the livestock sector to be more easily recognized as opposed to using any other conventional products which severely impair productivity in the breeding business. Besides this, an important patent was filed which depicts a novel and extremely gentle treatment procedure for the formidable "Graft versus Host Disease" (GvHD). This disease occurs when the immune cells of a transplant attack the host's organism. In almost half of all stem cell transplantations, this leads to medical conditions which are, in some cases, serious and life-threatening.

Which other technologies are being pursued by the department? We will definitely pursue Dr Ulbert's successful technology platforms on developing vaccines and strengthening resistance in the fields of both veterinary and human medicine. Moreover, in the department, Dr Schubert is investigating interesting plant compounds for oncological applications. Also, in other respects, we would like to step up the search for and validation of drugs in the future. In the course of this, a special role is played by substances which are able to influence the immune system as selectively as possible and lead to immunotolerance, meaning to the acceptance of transplanted foreign tissue.

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 54.

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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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Vaccine Technologies Unit

The unit is developing vaccines against a variety of infectious diseases for human and veterinary medicine. Primary activities include research on recombinant protein and DNA vaccines against viral zoonotic infections. In addition, diagnostic assays for the detection of infectious agents are being developed.

Ligand Development Unit

Modern therapeutic and diagnostic approaches demand novel highly specific biomolecules. We develop antibody and peptide ligands with modern combinatorial and proprietary methods. Our work comprises mapping individual immune response, binding sites of antibodies, identifying novel targets in particular on cell surfaces and binding sites of therapeutic or diagnostic relevant proteins. Our goals are the modulation of the immune system, the development of potential peptide and antibody therapeutics as well as the development 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 group 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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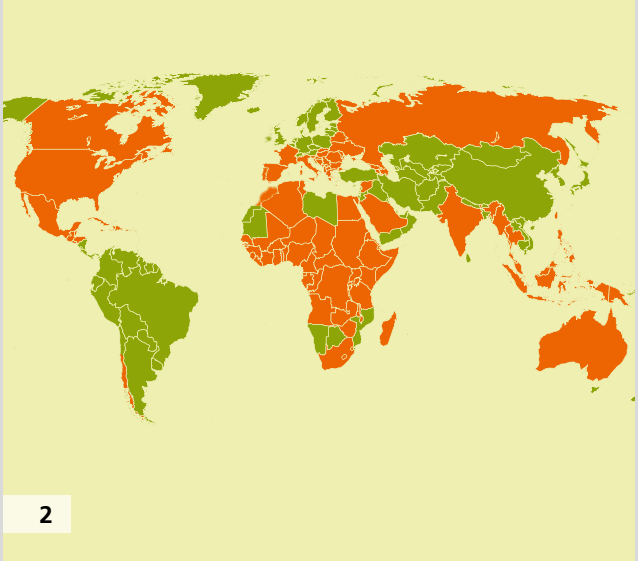

2

PROJECTS

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West Nile Shield Project
WINGS

SEVENTH FRAMEWORK PROGRAMME

EU project on combating the West Nile Virus

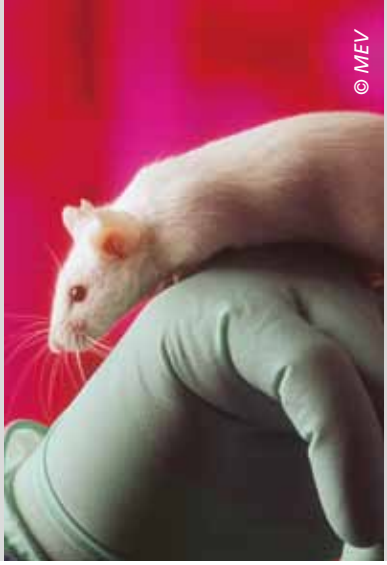
The past few years have witnessed an increasing emergence of West Nile Fever in Europe. This disease is triggered by the West Nile Virus (WNV), a zoonotic pathogen which predominantly affects birds, but can also be carried to mammals (most notably, humans and horses) through mosquito bites. Flu-like symptoms usually emerge, however in some cases severe, neurological courses of the disease are also observed. The infection is especially dangerous for older and immunodeficient people for whom it could be fatal. Greece experienced severe outbreaks in 2010 and 2011, with dozens of deaths and several hundred people taken severely ill. Increasing numbers of cases are also being reported in Italy, Hungary, Russia, Turkey and other Mediterranean countries. Furthermore, the West Nile Virus has been detected in birds in Austria and England. As some of the species of mosquito carrying the virus are also native to Germany, an outbreak of this virus in Germany can also not be ruled out.

At present, no vaccine exists to protect humans from becoming infected with WNV. In addition, it is difficult to detect the virus with an absolute level of certainty as the available diagnostics methods often cross-react with related viruses

The collaborative project "West Nile Integrated Shield Project (WINGS)", which has received three million euros in EU funding, is a response to the need for effective strategies to combat the virus. The overriding aims of this international collaborative project are to develop a particularly effective vaccine and to put improved systems in place to detect a WNV infection. As WNV is found in several variants in Europe, some of which are new, the technologies developed must be quickly adaptable to varying types of pathogen. In order to discover more about the variability of the different pathogen strains, the spread of WNV in Europe is being investigated epidemiologically. Under the coordination of the Vaccine Technologies Unit at the Fraunhofer IZI, nine partner institutions from Europe and the USA are working together until 2014 to implement the aims of the project. Besides the inclusion of prominent, internationally recognized virologists and immunologists, the consortium is also made up of companies active in the vaccine industry and is incorporated into several EU research programmes which focus on investigating and combating WNV.

1 *The West Nile Virus is transferred to birds and mammals through mosquito bites.*

2 *Following pandemics in North America, Africa and Asia, the West Nile Virus is also on the increase in Europe.*



Development of assays

Last year, units at the Department of Immunology successfully developed assay systems in several areas both independently and in collaboration with partners. Such systems are merely examples of the various possibilities of the department to develop multi-faceted detection methods for preclinical and clinical research through cross-unit collaboration.

A patent on new fragments of the PRRS virus was the starting point for developing an assay by the Vaccine Technologies Unit, together with the company AJ Roboscreen GmbH, for the safe and differentiated detection of this swine disease which causes billions of euros worth of damage worldwide. It is expected that this assay will come onto the market in 2012 and, based on the demand already being observed, has the potential to be a huge success for the industry partner. The Vaccine Technologies and Ligand Development Units offer versatile ways of developing new detection procedures in this area.

A further example is the development of GLP-compliant immunohistochemical detection of the MUC-1 antigen in histological cross-sections of ovarian carcinoma for the Australian company Prima BioMed Ltd. The histological cross-sections from patients included in the international phase II clinical trial at all study sites are being reviewed for suitability at the Fraunhofer IZI for the company's novel immunotherapy. This should prevent the development of metastases. Through this work, which was brought to GLP standard, the Fraunhofer IZI's histological laboratory could once again demonstrate its competencies.

Likewise, other alternatives to animal models were also developed further. A murine in vitro model was developed by the Immune Tolerance Unit which is able to examine the development of skin GvHD (see page 33) and its pathophysiology. In addition, new drugs with respect to the prevention or treatment of GvHD can be tested ex vivo. In order to assess the manifestation of GvHD, cytokine analyses and molecular biological investigations are carried out besides the histological and immunohistological analysis (e. g. CD95). The results of these investigations show that the murine in vitro skin GvHD model is comparable with in vivo data and is therefore suitable for analysing the progression of GvHD. Due to the multi-factorial parameter of GvHD, investigations on the gastrointestinal tract should be made possible in future using this in vitro model. In the long term, the model could be used in human transplantation medicine to receive information on the probability of GvHD and its degree of severity before transplantation.

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Mapping immune response

Modern Phage Display technologies at Fraunhofer IZI allow the use of peptide libraries in the scale of 10^{10} sequences and beyond, e. g. by applying in vitro recombination more than 10^{15} sequences are accessible. With these not only standard applications but also completely new tasks can be tackled.

A routine application of phage display is mapping monoclonal antibodies. This allows the identification of binding peptide sequences. These do not only give detailed information regarding the binding site of the antibody but they are, for example, useful in sorting clones of monclonal antibodies. The identified sequences are often similar or identical with the antigenic region of the protein sequences. Conformational epitopes can be identified with special software tools. In addition these peptides are efficient in affinity purification procedures and for robust diagnostic devices.

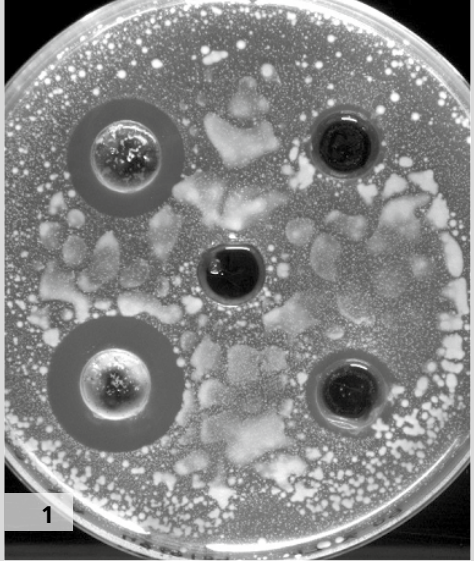
The size of the libraries allows mapping even more complex mixtures. We have been characterising a mixture of autologous antibodies derived from a patient for a company. Such peptides could be used for the generation of immune absorbers devices that help to remove the pathogenic auto antibodies from the blood of the patients.

The development of methods in collaboration with the Centre for Environmental Research, Leipzig is much more demanding. We use sera from atopic patients without any purification and could identify numerous peptides with high similarity to or even identity with known allergens. Similar procedures have been attempted many times with standard phage display libraries but besides a few successful exceptions they have not been very successful. At Fraunhofer IZI the success is based on thoroughly optimising the selection procedure in combination with an improvement of binding sequences by in vitro recombination of the peptide genes.

The collaboration with the Centre for Environmental Research aims at developing diagnostic tools for the early discovery and preventive treatment of allergies. Especially for children genetically predisposed to developing allergies such tools would be of immense value.

1 *The early detection of allergies is to contribute to preventative therapy concepts.*

2–4 *The creation of huge peptide libraries based on bacteriophages (> 10^{10}) requires special processes, just as the characterization of protein interactions is an important component of our work.*



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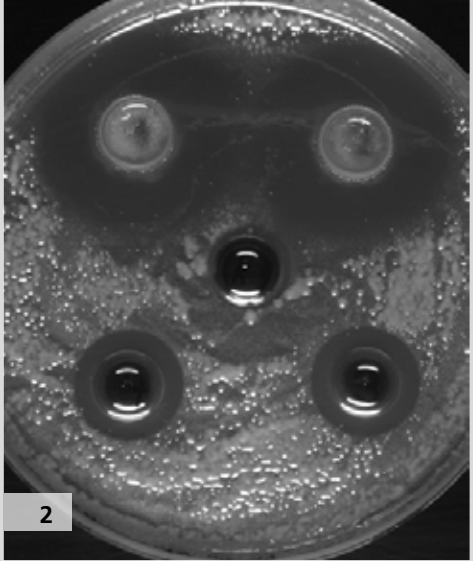

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Bioactive Compounds

The increasing development of resistance in pathogenic micro-organisms during the course of conventional treatment with antibiotics is becoming more and more problematic, particularly in the treatment of bacterial infections. Today, all around the world, resistances to nearly every type of antibiotic are described for all hospital germs.

Therefore, science and the pharmaceutical industry are facing the huge challenge of either developing new antibiotics within a narrow timeframe, or establishing treatment alternatives. In doing so, the use of bioactive substances may provide a promising approach (e. g. antimicrobial peptides, antibiotic plant compounds) in the fight against multi-resistant germs. Antimicrobial peptides are an important component of the innate immune system of low eukaryotes, plants, insects, and amphibians right through to humans, and serve to ward off microorganisms such as bacteria, fungi and viruses.

Antimicrobial peptides were first identified in frogs and insects in the 1980s; the number of known antimicrobial peptides currently amounts to 1 200. After identifying peptides exhibiting a bactericidal or fungicidal effect, a number of amino acids were substituted within these peptides, with the aim of improving their efficacy. In the Vascular Biology Unit, several antimicrobial peptides have been developed using this method, which, under in vitro conditions, kill all relevant multi-resistant hospital germs more efficiently than the antibiotics used until now. In further investigations (e. g. in murine infection models), efficacy and / or tolerability are now being tested under in vivo conditions. Antimicrobial peptides could be used in various ways – as antibiotics as well as in the food and cosmetics industry.

In the earth's tropical belt, plants have developed various strategies to defend themselves against micro-organisms. Besides having a powerful antibiotic effect, some of these substances also have the potential to effectively damage tumor cells. In cell culture experiments it was proven that non-tumor cells (e. g. endothelial cells and fibroblasts) are significantly more resistant than these tumoricidal compounds. On the basis of these findings, a new tumor drug is to be developed from these plant compounds over the next few years. In collaboration with partners, primarily from Africa but also from Central America, further plants with antibiotic and / or tumoricidal compounds are currently being analyzed at the Fraunhofer IZI.

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

1

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Future Markets – SteriHealth

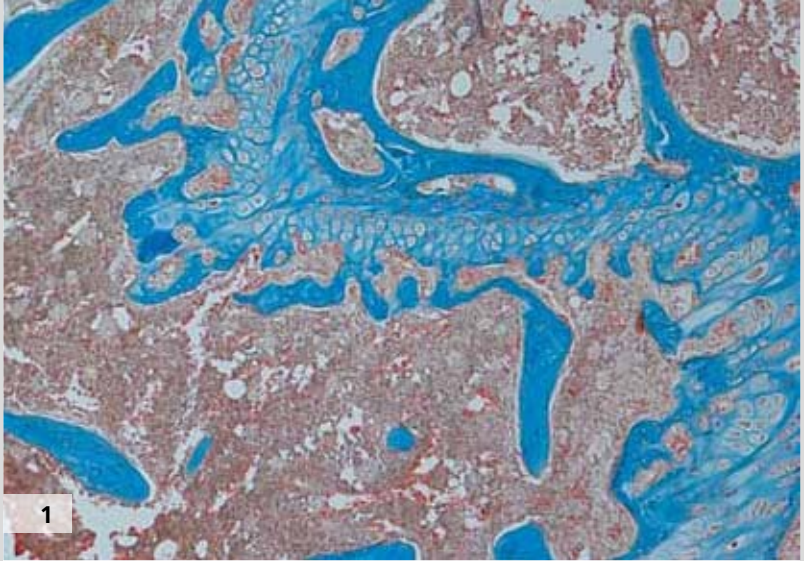
In the German healthcare sector, costs amounting to around seven billion euros are caused by secondary infections. Every year, up to 800 000 patients become infected whilst staying in hospital, usually with antibiotic-resistant germs (e. g. MRSA and NDM-1). Hospital germs are responsible for around 40 000 deaths per year in Germany alone. Therefore it is of absolute urgency that the hygiene control measures currently in place continue to be improved.

The SteriHealth project aims to develop a highly effective hygiene control process, with a particular focus on thermolabile instruments, implants and cell therapeutic preparations. This hygiene control process comprises all components, starting with the development of an optimized sterilization cycle followed by providing evidence of a germ-free environment and / or the absence of endotoxins on packaged products right through to the point at which these products are removed from their packaging in the medical practice or hospital. This development process is to culminate in the creation of a "mini steriliser", which will allow medical devices that previously could not be sterilized, or only with great difficulty, to also be sterilized on-site within a matter of seconds, using physical radiation technology which is both gentle and highly effective (e. g. electron beams).

The competencies of six Fraunhofer Institutes have been brought together to implement this highly demanding task. Besides the Fraunhofer IZI, project partners are the Fraunhofer FEP, the Fraunhofer IBMT, the Fraunhofer ITEM, the Fraunhofer IVV / AVV and the Fraunhofer IZFP. For this project, antimicrobial peptides are to be developed at the Fraunhofer IZI which, when deposited onto the surfaces of packaging materials or if immobilized, will not be impaired by the sterilization process in terms of their structural integrity and will thus allow a germ-free environment for the sterilized products, even over an extended period of time. Furthermore, the antimicrobial peptides to be developed are expected to exhibit a low level of cytotoxicity compared with human cells, which would possibly also facilitate their application in the area of new antibiotics.

The mini steriliser is primarily to be used in doctors' surgeries, retirement homes and, where appropriate, in hospitals.

1 / 2 *New strategies in fighting antibiotic-resistant germs are primarily required in the clinical field.*



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Human CD4 antibody therapy in stem cell transplantation

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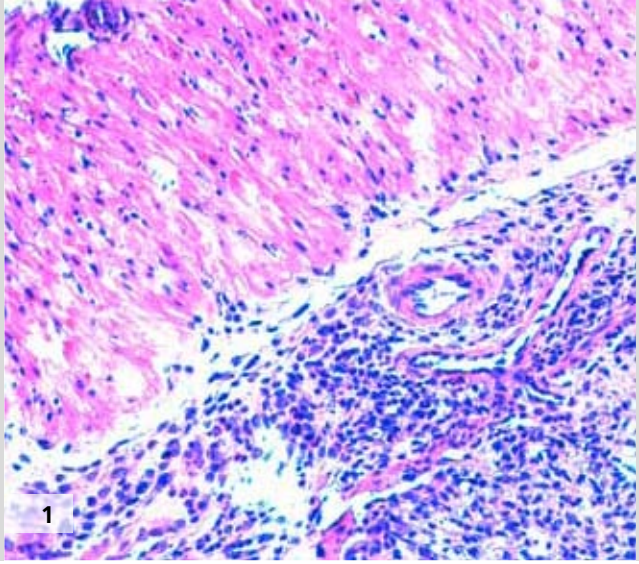
Often the hematopoietic stem cell transplantation (HSCT) is still associated with a variety of serious life-threatening complications (bacterial, viral and fungal infections). The main complication is the so-called Graft-versus-Host Disease (GvHD) and affects up to 80 percent of patients. Here, the T cells of the graft tissue recognize the recipient tissue as foreign and destroy it. Unfortunately, current treatment options using immunosuppressive drugs (Cyclosporine), or monoclonal antibodies (OKT3 ®) are very limited, many have side effects and lead to a suppression of the entire immune system of the compromised patients. It is therefore particularly important to develop specific therapies leading to immune tolerance induction in patients without disturbing other important immunological processes to ensure the survival of patients. For this purpose, particularly specific antibodies are suited, which could suppress the immune activity of CD4+ T cells over a short time period. CD4+ T cells play a major role in the development of GvHD after HSCT.

Therefore, the aim of the group is to optimize the therapy and testing of the human CD4 antibody for the potential immune tolerance induction using the murine hematopoietic stem cell transplantation model, which was established in recent years. Humanized mice (huCD4+ muCD4-, HLA-DR3+) serve as donors and wild-type mice as recipients. This allows the direct testing of human CD4 antibody in a murine model. In numerous in vitro and in vivo immunological experiments different parameters (e. g. proliferation, cytokine release) or toxic effects were investigated.

The in vivo data convincingly demonstrate that immune tolerance was induced in the graft and GvHD was prevented. Compared to non-treated mice anti-human CD4-treated recipients show nearly 100 percent survival without any symptoms of GvHD and engraftment of donor cells in the bone marrow after HSCT. The regenerated hematopoietic system shows characteristics of the donor (full donor chimerism).

This suggests that the developed strategies may represent a new therapeutic option in transplantation medicine for the prevention of GvHD, which is simple to implement. Perhaps this may also be a therapeutic alternative for patients who are refractory to conventional immunosuppressive therapies. The graft-versus-leukemia effect was not affected negatively. Long-term use in the field of solid organ transplantation (e. g. skin) and autoimmune diseases is conceivable.

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



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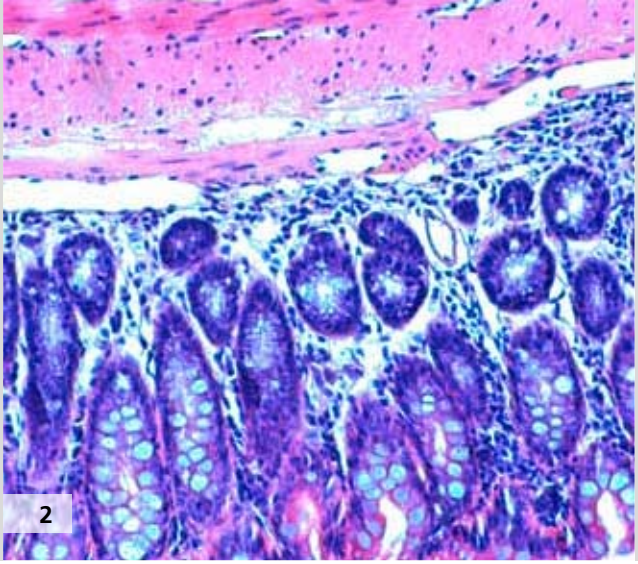

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Extracorporeal bowel model system: Novel tool for the development of epithelial barrier-stabilizing therapy strategies

Crohn's disease (CD) and ulcerative colitis (UC), collectively termed inflammatory bowel diseases (IBD), represent chronic relapsing and remitting inflammatory disorders of the gastrointestinal tract that are characterized by leukocytic infiltration of the intestinal mucosa and submucosa. Research over the last couple of years has led to great advances in scientific discovery and has expanded our understanding of IBD and their underlying pathophysiological mechanisms. Studies have provided evidence that IBD is a result of a genetic predisposition that leads to a mucosal immune regulatory cell defect, barrier defects, and susceptibility to environmental triggers, including luminal bacteria and specific antigens.

Approximately 300 000 people in Germany suffer from IBD. Anyone can be affected regardless of gender. Typically, the condition afflicts those who are between the ages of 15 and 35. There are also cases however where elderly and very young children suffer from the disease. Currently, there is no cure for IBD. Thus, people must undergo a lifelong drug treatment and / or surgical care. The goal of treatment is to control the disease by (1) minimizing the number and severity of flares, (2) inducing and maintaining remission, and (3) preventing complications. Drug, biologic, and nutritional therapies are the foundations of treatment, but therapy must be tailored for each individual.

The aim of this project is to establish extracorporeal bowel model systems for the study of the underlying pathophysiological mechanisms and the development of novel therapy options. This model system consists of an intestinal segment that is cannulated, perfused in situ, and maintained in an isolated circuit. This extracorporeal loop maintains physiological conditions for an extended time period and allows for investigating cellular responses of apical mucosa cells on luminal applied substances. In addition, direct effects on intestinal epithelial cells as well as myeloid and lymphoid cell populations were analyzed. These analyses allow the estimation of the therapeutic potential of the substances.

The establishment of other extracorporeal model systems for the analysis of the interplay between bacterial, food allergens, food additives, and potential toxic substances with an extracorporeal bowel segment is intended in the future.

1 *Hematoxylin and eosin-stained colon section of mice suffering from dextran sulfate sodium (DSS) -induced colitis.*

2 *Hematoxylin and eosin-stained colon section of mice recovered from dextran sulfate sodium (DSS) -induced colitis.*

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2

Purification and storage of phagocytic cells from human blood for therapeutic use in man

Granulocytes and monocytes represent the most important phagocytic immune cells in humans. In severe inflammation and sepsis the number of mature well-functioning phagocytes may be severely reduced. The therapeutic use of human donor granulocytes is limited at present, due to a lack of sufficient immune cell mass and high percentage of other blood cells in the donations. Moreover, complicated donor logistics and a lack of storability hamper a wider clinical application. Technically, already today granulocytes and monocytes can be provided as so-called granulocyte concentrates by specialized blood banks.

In this project human granulocytes / monocytes will be purified from regular granulocyte concentrates to yield highly purified cell concentrations. The purification and subsequent storage will be performed to allow later use in therapeutic medicine. It will be evaluated for how long such purified cell concentrates can be stored with sufficient viability and functionality. In this context various storage conditions will be tested, e. g. temperature, movement, tubing and storage bag materials as well as storage fluids. Moreover, cryo-conservation of the ultra-pure cell concentrates will be evaluated as well.

In cooperation with the biomedical technology company Artcline GmbH, Rostock, Germany we will work towards the first clinical use of the new cell product. Artcline (www.artcline.de) has developed and clinically tested a bed-side cell-bioreactor device that enables the on line-perfusion of human donor granulocytes with the plasma of septic patients for several hours with the bioreactor's cells being strictly kept extracorporeal. Clinical results include the removal of bacterial toxins and improvement of cellular immune competence in the patients. These positive effects shall be further enhanced by the use of highly purified immune cell concentrates.

The successful establishment of a method for the purification and storage of granulocyte concentrates prepares the ground for further developmental projects. The working group is open for future cooperation in this field with interested partners from industry and / or research organizations.

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1 *Purifying granulocyte concentrations in syringes as downscaling experiments.*

2 *Granulocyte concentration in a manual blood press – upscaling experiments to develop practice-oriented methods.*

DEPARTMENT OF CELL THERAPY

IN CONVERSATION WITH DR. DR. JOHANNES BOLTZE

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As a result of the landmark decision made by the European Court of Justice in October 2011, embryonic stem cells and procedures for their manufacture are no longer patentable. What impact does this decision have on the work of the Cell Therapy Department? Embryonic stem cells are primarily of therapeutic interest. A level of patent protection on therapeutic procedures which is too extensive would, theoretically, open up the opportunity to withhold certain types of therapy from certain patients – this cannot happen. In this respect, the decision cannot be completely opposed. For those of our units working in the field of therapy development, however, no impacts are primarily connected with the decision as we mainly use adult stem cell populations and also research far beyond the boundaries of pure cell therapy. In recent years, Dr Stolzing's unit has indeed managed to develop and patent a procedure to manufacture induced pluripotent stem cells. These cells are very similar to embryonic stem cells and are normally produced by the infiltration of so-called pluripotency factors in mature somatic cells through viruses, which of course, limits their use in the clinic. Dr Stolzing's procedure does not require viral vectors and is therefore fundamentally suitable for therapeutic application.

Which of the Department of Cell Therapy's achievements in 2011 are you particularly proud of? Besides a number of really terrific academic degrees gained by our staff at various levels, through to dissertations and numerous high-ranking publications, we are particularly proud of acquiring the Legascreen project. This deals with the development of new diagnostic procedures for dyslexia. The project will be implemented together with partners of the Max Planck Institute for Human Cognitive and Brain Sciences in Leipzig. Another significant success was the continuation of the Zellwerk project under the guidance of Professor Walles, in which Dr Stolzing's unit is substantially involved.

Which events are you particularly looking forward to in 2012? In May, our "7th International Symposium on Neuroprotection and Neurorepair" will be held in Potsdam. We have been hard at work preparing for this symposium for nearly two years. We are looking forward to welcoming over 40 of the world's leading scientists in our field. That will definitely be a highlight. We are also looking forward to a number of highly interesting cooperation projects with academic partners and industry which, by the way, go far beyond pure cell therapy.

With the completion of the first extension building also comes an expansion of the Department of Cell Therapy's research infrastructure. What impact will this have on the department's future work? For nearly six years, a large proportion of our department has been reliant on the hospitality of other institutes at the University of Leipzig. This has obviously involved serious bottlenecks in the availability of laboratory space and infrastructure. Once the first extension building has been completed, as of the middle of 2012, we will finally have long-awaited access to this urgently required infrastructure. In addition to this come means of access to important technologies such as high-field magnetic resonance imaging which we are, of course, happy to share with our former hosts. In all, we are expecting a distinct increase in productivity in 2012.

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
- Behavioral phenotypic investigations
- Therapeutic monitoring and imaging (ultrasound, CT, MRT, PET, bioluminescence)
- Pre-clinical study design and quality assurance
- Histological investigations and cell diagnostics
- Evaluation of diagnostic and therapeutic procedures for cerebral and myocardial diseases
- 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 55.

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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.

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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Neuro- / Cardiorepair 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 models to small and large animal models. The implementation of strict quality standards increases the predictive value of preclinical research and may thus improve the translation of promising therapies toward the clinic.

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1

PROJECTS

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Genetic basics of dyslexia – Development of a test for the early diagnosis of reading and writing disorders

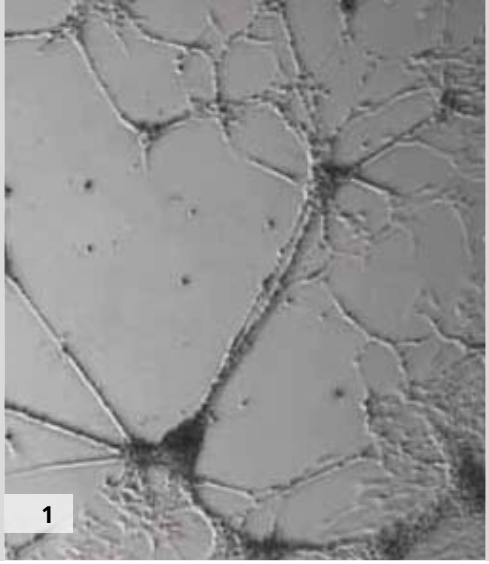
Dyslexia is a severe reading and writing disorder affecting about 5 percent of all German schoolchildren and therefore being one of the most common developmental disorders in childhood and youth. Dyslexia occurs independently of the child´s intelligence and causes tremendous problems at school, in education, and in the workplace. One of the main problems hampering successful therapy is the late diagnosis, because with the current methods, dyslexia can be reliably diagnosed not before the end of the 2nd grade. At this point, a large part of speech development has already taken place and a lot of time for early therapy has been lost.

Our aim is to develop a genetic screening test for dyslexia, applicable much earlier than current methods and therefore leading to increased chances for successful therapy and functional regeneration. Genetic dyslexia markers necessary for this test are identified in a micro array based fine screen supplemented by polymorphisms of highly relevant candidate genes. These markers are validated by A) genotyping an independent cohort; B) by characterising markers in functional magnet resonance imaging (fMRI) and C) by characterising markers in allele specific mRNA-expression analysis. The final test will neither include fMRI nor expression analysis.

This test translates genetic findings into a clinical assay. It will allow the early identification of children at risk, enabling early support resulting in functional regeneration.

Based on the cooperation with the Max Planck Institute for Cognitive Brain Sciences, fund-raising for a large follow-up project named LEGASCREEN was successful. This project unites the expertise of both institutes and will continue and extend the current project. This further strengthens Leipzig as a location of high-quality dyslexia research.

1 *An early test to diagnose dyslexia should enable preschool support for affected children and make starting school easier.*



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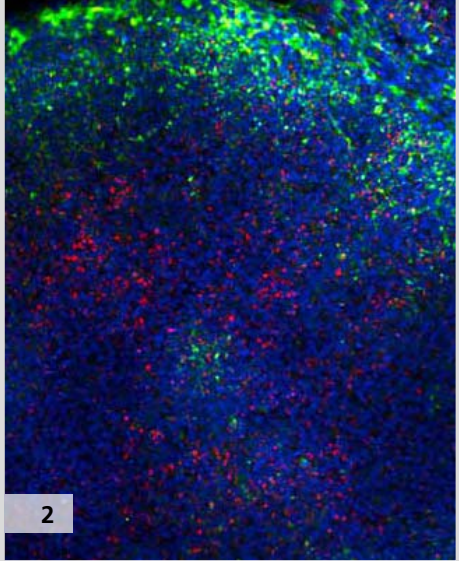

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Induced pluripotent stem cells from mRNA reprogrammed cells

Modern medicine has its hopes pinned on stem cells. Here it is predominantly the fact that stem cells are able to develop into as many different types of cell and tissue as possible that is of particular interest to medical research. Until now, embryonic stem cells were therefore viewed as the promising resource for pluripotent stem cells. Embryonic stem cells are capable of developing into any type of body cell and also have an extremely high capacity to divide. In order to obtain embryonic stem cells, however, blastocyst stage embryos have to be destroyed, which is why this research is, in itself, extremely controversial with regards to ethics. Work involving embryonic stem cells is regulated to variable degrees in the countries belonging to the European Union. Particularly strict regulations apply in Germany. In October 2011, a landmark decision was made by the European Court of Justice which prohibited the patenting and commercialization of human embryonic stem cells and procedures used to obtain such cells.

The ethical dispute and the given conditions call for an alternative in order to keep up with international research and medical advancement. Induced pluripotent stem cells (iPS) are very similar to embryonic stem cells in terms of their capabilities and characteristics. By means of a so-called reprogramming of somatic cells, a state is achieved which allows the iPS to be differentiated into nearly every type of cell. Most ways of manufacturing iPS, however, use viruses or viral factors, thus excluding medical application.

At the Fraunhofer IZI, a reprogramming method has been developed which is based on mRNA and does not involve permanent changes in the genome. Thus, iPS can now be manufactured with a high level of medical potential. Patient-specific stem cells may be used in cultivating tissue for regenerative therapies. Initial applications are, however, also thinkable in the areas of pharmacological development and toxicology.

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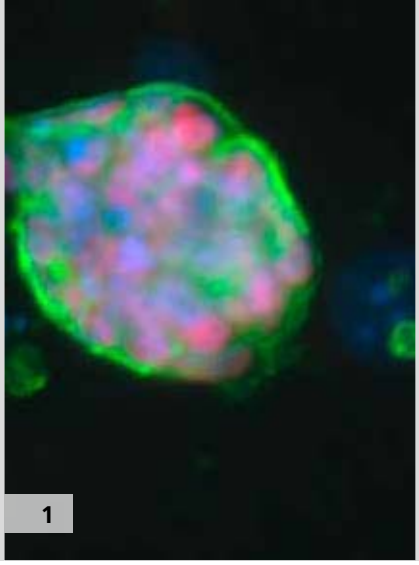
1 *Human iPS cells which were differentiated into neurons.*

2 *Human, pluripotent iPS colony.*



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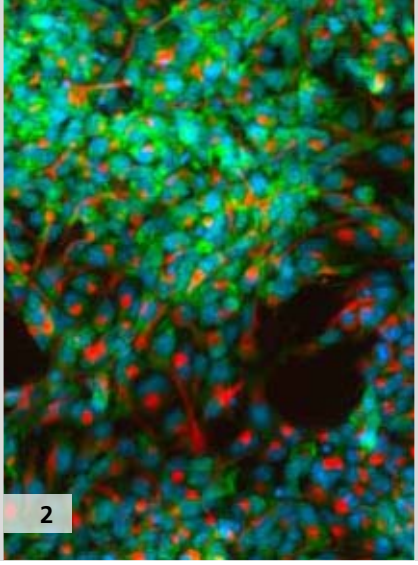

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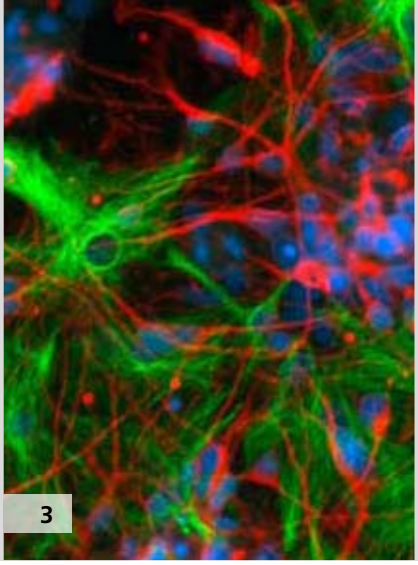

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Treatment of neurodegenerative diseases using custom-made neural stem cells

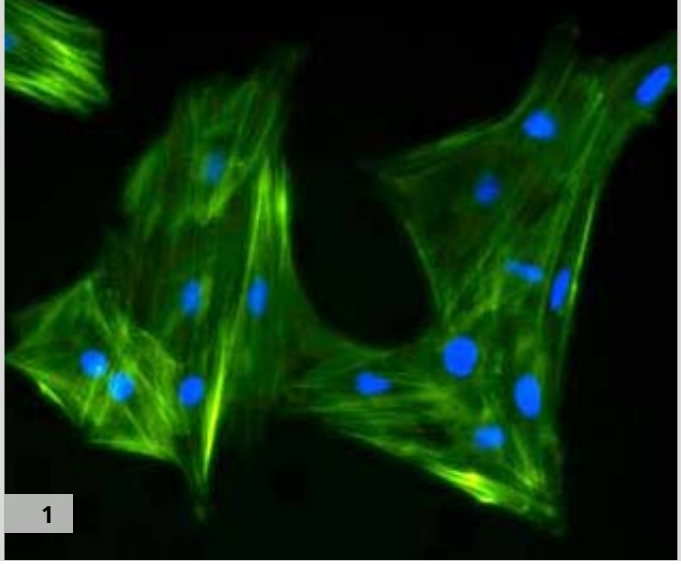
Modern therapy concepts for numerous diseases are based on the application of stem cells. Besides the ethical issues surrounding the use of embryonic or foetal cells, it has, however, also become apparent that positive effects, especially in terms of diseases affecting the central nervous system (CNS), are based on immunoregulatory mechanisms. Therefore, the application of autologous cells is being targeted for investigations into both therapeutic potential and the underlying mechanisms of action. As autologous neural progenitor cells are, however, normally unavailable, ways to manufacture pluripotent stem cells from somatic cells are to be established in the current project. Under the right culture conditions, neural progenitor cells can then be gained from these induced pluripotent stem cells and their therapeutic effect in a syngeneic model of CNS diseases can be investigated.

The findings which have emerged thus far allow the conclusion to be drawn that, besides species-dependant factors in generating and cultivating induced pluripotent stem cells, a detailed characterization and optimization of differentiation and reproduction of neural precursor cells are also of decisive importance as possible therapeutically effective cell populations. In further preclinical trials, besides identifying appropriate times for therapy, the appropriate cell dose and type of application are also to be optimized. Furthermore, potential mechanisms of action will be investigated more closely to contribute not only towards a better understanding of emergence and behaviour but, more specifically, towards the treatment options of CNS diseases.

1 *iPS colony.*

2 *Differentiation of neural stem cells.*

3 *Differentiation in mature astrocytes and neurons.*



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Cryoconservation of Mesenchymal Stem Cells Using Anti-Freeze Proteins

Cryopreservation is the most important method for preserving plant, animal and human cells and tissues with all vital functions. Cryopreservation is the key technology for the advance of regenerative medicine, tissue engineering and organ transplantation.

Freezing can damage cells due to ice cristal growth inside and between cells. The addition of cryoprotectant substances can minimise or block ice cristal growth but is often toxic. These additions can cause tissue damage. DMSO which is often used for cryopreservation has to be washed out when the material is transplanted to minimise side effects in the recipient. To minimize the addition of toxic substances we will investigate new cryopreservation substances.

Proteins leading to minimized ice cristal growth are called Anti-Freeze Proteins (AFP) or ice structuring proteins (ISP). AFPs are generated by a variety of organisms including animals, bacteria and plants. They allow plants to survive harsh winter temperatures. AFPs can bind to growing ice cristals minimising further growth of the cristal and thereby minimising cell damage. During thawing the AFP inhibit re-cristallization.

AFPs are especially interesting for cryopreserving stem cells or tissue engineering products such as skin and cartilage. Further applications include banks for plants, bacteria, sperm, eggs, embryos of endangered species or special transgenic animals or for food storage.

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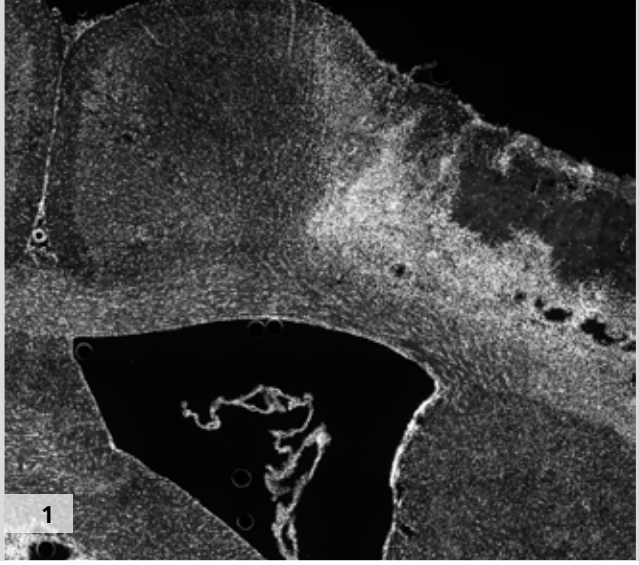
Europa fördert Sachsen.
EFRE
Europäischer Fonds für regionale Entwicklung

Gefördert aus Mitteln
der Europäischen Union

1 *Cryopreserved mesenchymal stem cells.*



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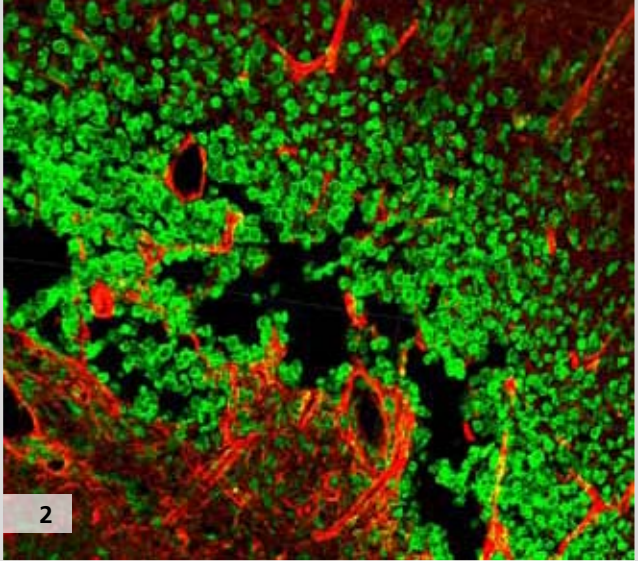

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Freshly-isolated adipose tissue-derived cells for acute stroke

Adipose tissue contains several stem cells and regenerative cell populations and is hence an interesting source for cell-based therapies. Regenerative cells from adipose tissue (ADRC) mediate angiogenesis and an increased expression of growth factors. Moreover, ADRC showed a profound immunomodulating effect in experimental models of inflammatory diseases. ADRC can be harvested in large amounts and with low morbidity; thus, these cells offer the unique advantage of an autologous cell population that is available very quickly post ictus.

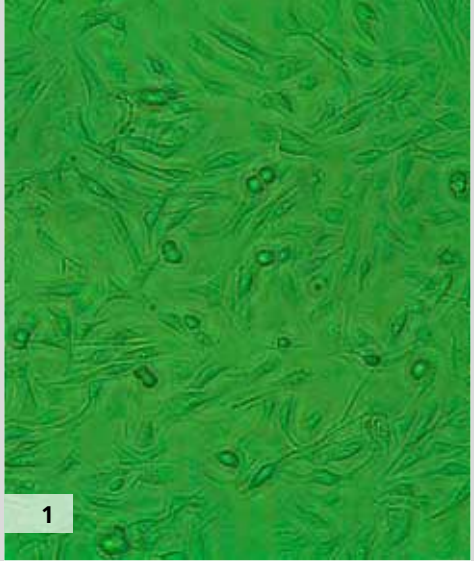
This enables cell therapies of acute diseases that need treatment within a limited time window. ADRC have been successfully applied in animal study of myocardial infarctions and clinical trials are ongoing.

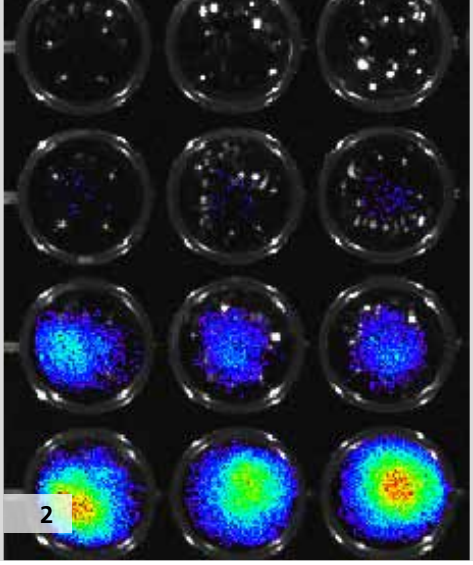
The goal of this project is the evaluation of therapeutic efficacy of adipose tissue-derived cells for acute cerebral ischemia. Cells are administered intravenously at different time points after experimental stroke. Efficacy of cell transplantation will be investigated depending on cell dose and therapeutic time window. The endpoints for successful cell treatment are neurofunctional improvement. Furthermore, infarct volume will be investigated serially and non-invasively using magnetic resonance imaging. After the experiments, brain specimens will be analyzed using immunohistochemestry and quantitative PCR to gain a better understanding of the underlying mechanisms of action.

If adipose tissue-derived cells is safe and effective after experimental stroke, it is aimed to translate this concept towards a clinical application.

1 *Cortical lesion after experimental stroke.*

2 *Inflammatory reaction in the periphery of the stroke.*





T-cell infiltration in tumor tissue

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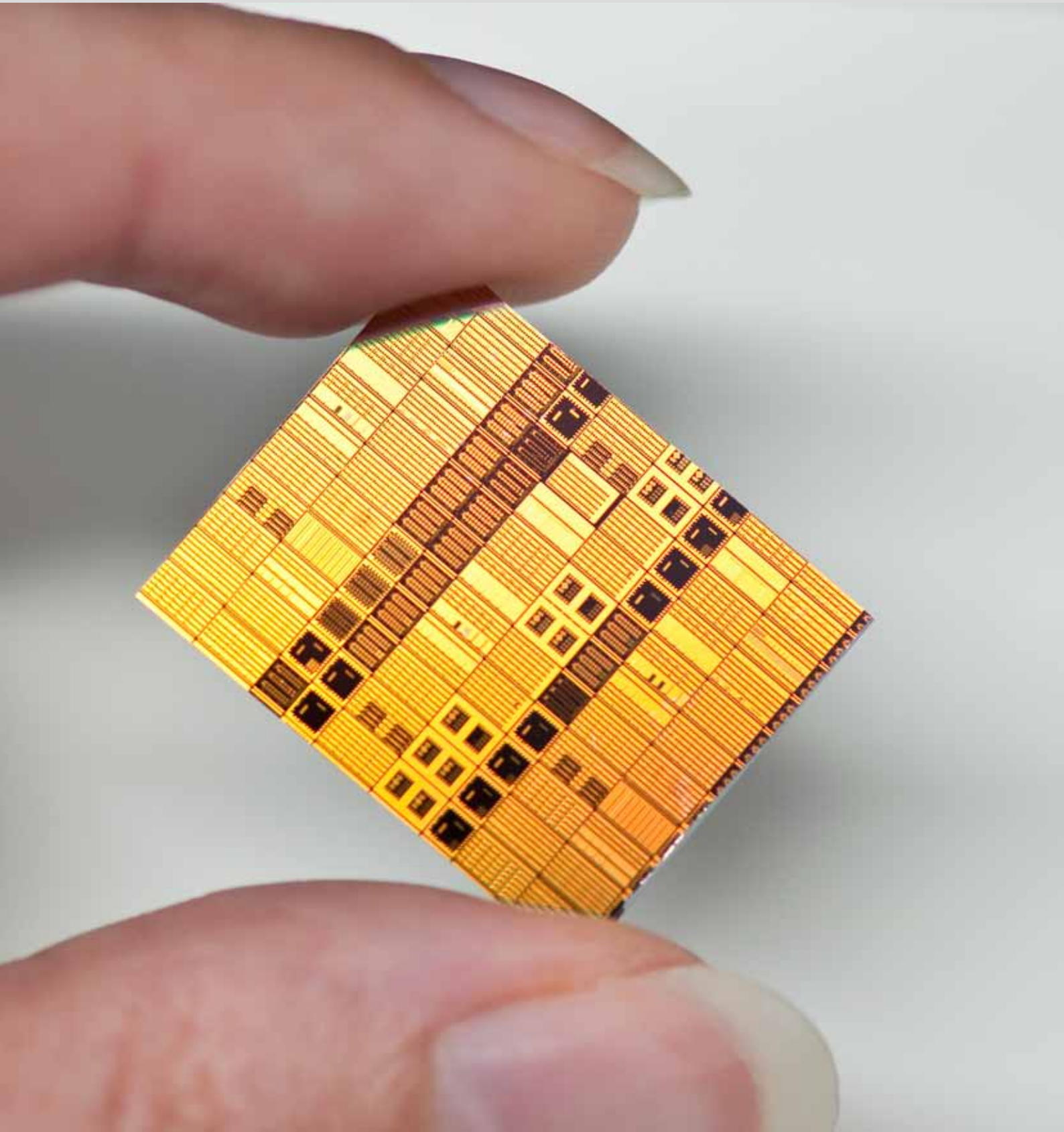
The increasing prevalence of oncological diseases necessitates a breakthrough in the discovery of efficient and affordable therapeutic procedures. The so-called cancer or tumor vaccines present an alternative to treatment strategies used until now, such as chemotherapy and radiation therapy which are associated with significant side effects and high costs. Tumor vaccines are based on the principle of the body's own immune defense. As tumors develop from degenerated body cells, they are usually not recognized by the immune system as being foreign or dangerous and therefore escape the immune defense. Cancer vaccines aim to change this state and modulate the immune system in such a way that tumor cells are specifically recognized and eliminated by the body's own immune system. Antigen-specific T cells play an important role in this process. In order for these cells to actually take effect, they have to penetrate the endothelium in order to reach the respective tumor cells. Initial investigations have already shown that increased T-cell infiltration is associated with increased longevity of cancer patients.

The project aims to shed light on the mechanisms which increase the migration of antigen-specific T cells to include them in the development of immunotherapeutic procedures. The initial investigation, in cooperation with the Clinical Oncology Department at the University of Nottingham (Professor L Durrant and Dr J Ramage), demonstrated strengthened trans-migration of tumor antigen-specific T cells by means of antigen-specific MHC-I recognition on endothelial cells. This supports the assumption that the endothelial cells absorb and present specific tumor antigens by means of intercellular peptide transfer through "gap junctions". Investigations are currently taking place to demonstrate the mechanism of antigen-specific T-cell migration in tumor tissue and the role of "gap junctions" in intercellular peptide transfer. As part of this research, the role of anti-angiogenic drugs which also modulate the formation of "gap junctions" and their influence on the migration of antigen-specific T cells will be analyzed.

1 *B16 melanoma cells (10x).*

2 *In vitro detection of tumor cells by means of bioluminescence imaging.*

DEPARTMENT OF DIAGNOSTICS



IN CONVERSATION WITH PROF. DR. FRIEDEMANN HORN

What were the greatest achievements of the Department of Diagnostics in 2011? Under the coordination of the Fraunhofer IZI, 2011 saw the start of the RIBOLUTION project – a research network funded by the Fraunhofer Future Foundation which consists of five Fraunhofer Institutes, several universities, and GlaxoSmithKline as an external partner. This project seeks to find new RNA biomarkers for various diseases, besides automating and perfecting the technology used for biomarker screening. A further success was achieved in demonstrating that three so-called microRNAs are disabled in the tumor cells in the case of prostate cancer. These "disabling switches" block certain signalling pathways in healthy prostate cells which lead to the unimpeded growth of tumor cells. The RNomics Unit could demonstrate that the tumor cells can no longer grow and die off when they are re-introduced to these microRNAs. This could form the foundation of a novel therapy strategy in dealing with this type of cancer. New strategies for treating cancer are also the subject of an EU project which the department successfully acquired together with the Department of Cell Engineering and the Spanish company Ikerchem, and which will begin in 2012. This project shall test the efficacy of innovative pharmaceuticals developed by Ikerchem, with the help of tumor cells and tumor stem cells which will be isolated by the Tumor Stem Cell Unit.

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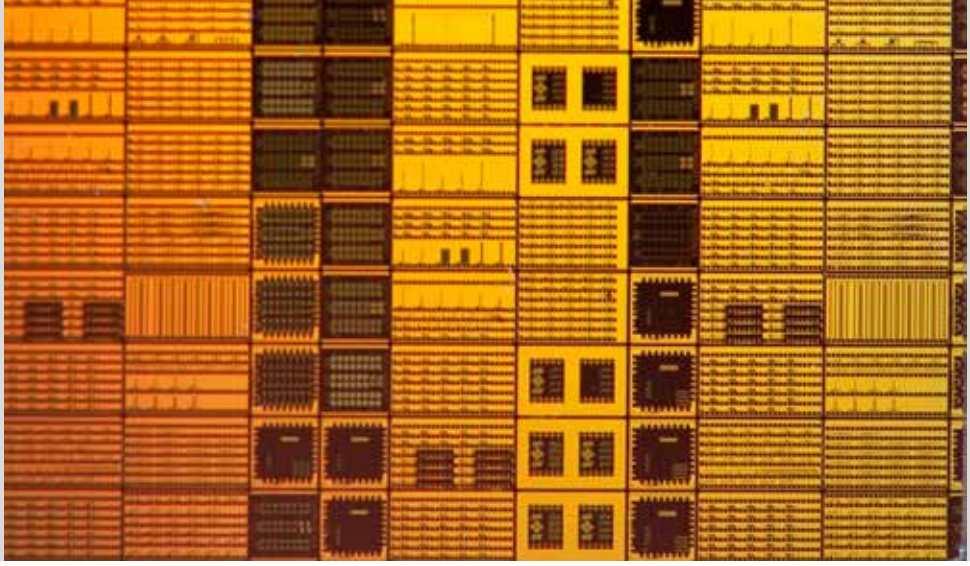
What exactly is new about the ncRNA technology and what types of application are you envisaging? Of the 3.3 billion bases of the human genome, only around two percent are necessary to code our repertoire of proteins. The remaining 98 percent were largely considered to be "junk DNA" which have accumulated 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 in fact 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 specifically 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 seen in the above example of microRNAs disabled in prostate cancer, which are also classed among ncRNAs, they are also highly interesting from a therapeutic point of view.

Which other core scientific themes is the department pursuing? In order to test new therapeutic approaches, cell culture and animal experiment models are being developed and applied in the department. Tumor stem cells and mouse models for rheumatoid arthritis form core themes in this regard. The development and application of molecular diagnostic technology is another area of competence in the department. Besides innovative immunoassays and genetic analyses, lab-on-a-chip platforms or test-strip-based rapid tests are also at the forefront here.

What are the department's objectives for the coming year? Besides striving to acquire further publicly funded projects and industry contracts, another major aim entails networking the different competencies and technologies within the department even more effectively and generating new, innovative approaches from this synergy.



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 55.

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Molecular Diagnostics 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.

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

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ParoChip

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 ParoChip 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 ParoChip 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.

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

1

2

RIBOLUTION – Integrated platform for the identification and validation of innovative RNA-based biomarkers for personalized medicine

Biomarkers are molecules or parameters, which can serve as diagnostic disease markers that indicate incidence and progress of a disease or predict its response to treatment. An early diagnosis may help to prevent progression to disease states that are difficult to treat. Improved differential diagnosis allows choosing the optimal therapy for the individual patient. Hence, there is an urgent clinical need to identify novel biomarkers.

Recent research has demonstrated that the overwhelming part of the human genome is not used to encode proteins. Such "noncoding" parts of the genome had initially been regarded free of information and futile. Today, however, it is known that these sequences give rise to a giant number of so-called noncoding RNAs, ncRNAs, which play a pivotal role in cellular regulation. A growing number of such ncRNAs is now being recognized as disease-associated. Therefore, they represent a gigantic and so far almost unexplored pool of potentially valuable biomarkers for medicine.

RIBOLUTION is a research network of five Fraunhofer Institutes in cooperation with several universities and is funded by the Fraunhofer Future Foundation. By a comprehensive genome-wide screening programme, RIBOLUTION aims at identifying such novel RNA biomarkers and at validating them as diagnostic tools. This approach will be applied to a number of selected, exemplary diseases. Amongst them are prostate carcinoma, which with a Europe-wide incidence of annually 350 000 cases represents the most frequent cancer disease among men, and chronic obstructive pulmonary disease (COPD), which currently represents the fourth most common cause of death. Worldwide, up to 600 million people suffer from COPD, with almost 15 percent of people aged 40 and older being affected in Germany. For both diseases, novel biomarkers able to predict progression and to aid therapy choice are urgently needed. Biomarker screening in RIBOLUTION will be carried out using tumor samples from prostate cancer patients in collaboration with the University Hospital of Dresden, and using samples provided by the international COPD study ECLIPSE funded by GlaxoSmithKline.

In addition, the research network RIBOLUTION will develop technical innovations to optimise and improve the biomarker screening process itself to render this process more reliable and more economic in future.

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1 / 2 *Biomarker screenings with modern high-throughout techniques such as microarrays.*

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-complaint manufacture and testing of cell-based therapeutics (ATMP, tissue preparations) for clinical trials
- Development, validation (pursuant to ICH Q2A/2B and the European Pharmacopoeia) and conduct of quality controls for cell-based therapeutics
- Support in structuring GMP-complaint manufacturing processes (e. g. process transfer, validation pursuant to appendix 15 EU GMP guidelines)
- Antibodies – Monoclonal / polyclonal
- Customized development and validation of immuno-logical 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

- Human immune system in the animal model (murine)
- Model of Graft versus Host Disease (in vivo / in vitro)
- Model of inflammatory bowel disease (murine)
- Development of vaccines (antigen, expression systems, adjuvants) for human / veterinary medicine
- Vaccine monitoring (development of tests)
- Antibody development / characterization
- Phage display with peptides
- Antimicrobial peptides
- Bioactive natural products
- Strengthening the intestinal barrier
- Cellular bioreactors for septicaemia treatment
- Extracorporeal circuits and functional studies
- Cell separation processes
- Cell / tissue preservation
- Cellular biobanks

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michael.szardenings@izi.fraunhofer.de

Department of Cell Therapy

- Optimization of the cryopreservation of cells and tissue
- Reprogramming of cells – iPS (induced pluripotent stem cells)
- Screening for anti-ageing and tissue-regenerating drugs
- Testing stem cells in neurodegenerative models
- Differentiation of iPS in neuronal and glial cells
- Testing pluripotency
- Establishing stable iPS reporter cell lines
- T-cell infiltration patterns in vitro and in vivo
- Developing prototypes
- Cytotoxicity assays
- Cell sorting
- Model systems myocardial ischemia – rat / mice
- Stroke model systems: rat / mouse
- Experimental imaging
- Histology of the mammal brain
- Large animal model (sheep) for cerebral ischemia
- Cell culture models
- SNP analyses of the human genome

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Department of Diagnostics

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

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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 modern institute building was completed and put into operation in 2008. As well as excellent working conditions, the building offers institute personnel a communicative infrastructure, prompting interdisciplinary exchange between units. A spacious seminar area and a prestigious atrium also cater for various advanced training formats and scientific events to be held, such as the "Fraunhofer Life Science Symposium".

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 institute's facilities. A flexible cluster structure allows laboratory sections to be adapted and fitted out in line with the specific requirements of a broad range of projects. 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. The institute occupies a 2 300 m² laboratory area and a 1 400 m² office area.

Clean room facilities (GMP)

In the neighboring BIO CITY the Fraunhofer IZI operates a GMP facility for the manufacture of cell-based medicinal products for clinical studies. The GMP area covers 450 m² and is divided into different suites. In its clean rooms, work can be carried out under cleanliness class A. The suites are fitted with different types of equipment in order to meet different performance requirements. The facility's modular structure allows different projects to be handled in parallel and independently of one another.

Extension building

The Fraunhofer IZI is currently constructing an initial extension building. With this building, the institute's laboratory capacities will be extended by around 1 200 m². The extension includes a considerable experimental medicine area suitable for establishing and testing small and large animal models. An expansive equipment pool for all kinds of imaging procedures (e. g. magnetic resonance imaging) completes the research unit. The institute's clean room capacities will also be expanded by the new building. The GMP manufacturing area will be increased by around 450 m² to a cover a total area of 900 m². Through this extension, the institute is reacting to the constantly growing demand within the area of clinical trials of cell therapy procedures. The completion of the first extension building is planned for mid-2012. A second extension building is currently in the planning stages.

Excerpt of the equipment pool at the Fraunhofer IZI

Cell biological

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

Molecular biological

- Affinity measurements (BIACORE)
- Expression analysis system
- High pressure liquid chromatography (HPLC)
- Mass spectronomy
- Microarray scanner and hybridization stations
- PCR and electrophoresis park (e. g. real-time PCR)
- Proteom analytics
- Reporter gene measuring (Luminometer)

Imaging

- Bioluminescence imaging
- Fluorescence- / confocal microscopy
- Immunohistochemistry / histology

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
- 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

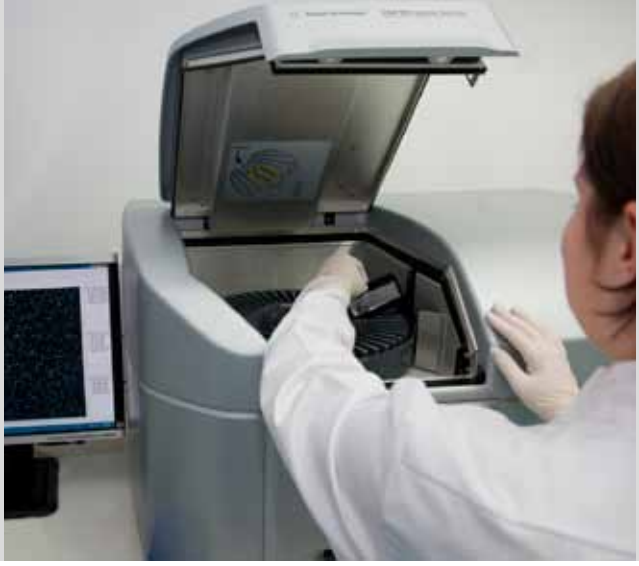
Antibodies identify antigens through a highly specific binding. This makes them interesting tools in biology, medical research and in both treatment and diagnostics.

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
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 preclinical and clinical trials require valid high throughput analysing 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 varied 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 for and together with the partner. The modern, high level 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 diagnostic and monitoring. Therefore the complete value-added chain, 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 ncRNA has recently become more important as they 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 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).

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Cultivation of pathogens

Display of antigens

Design of vaccine vectors / proteins

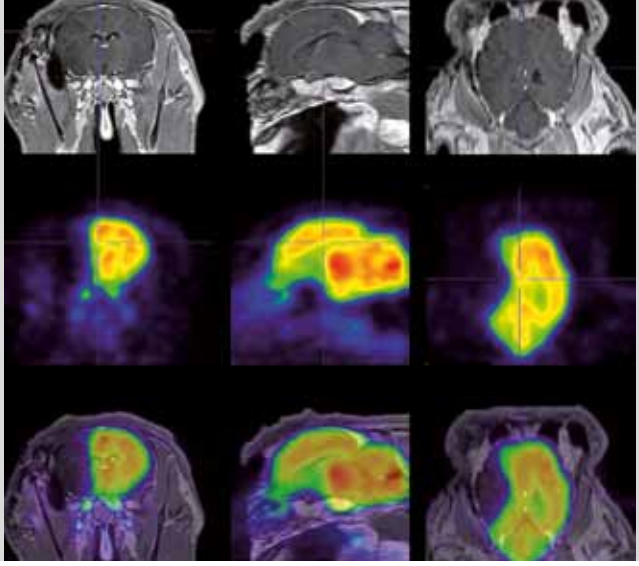
Small animal models for immunizations

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

QUALITITY 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 law and anchored in the chemical law ("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 m² 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 therapies medicinal product and tissue preparations). 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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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 eight 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 around 8 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.

- **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.

- **Prima BioMed GmbH** (settled in 2010)
  - Origin: Australia, Prima BioMed Ltd.
  - Business model: developing an immunotherapeutic to treat ovarian cancer.

- **Sonovum AG** (founded in 2011)
  - Origin: Germany, Fraunhofer IZI
  - Business model: developing diagnostic procedures on the basis of ultrasounds.

PARTNERS

SCHENKE LEBEN, SPENDE BLUT.

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.

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.

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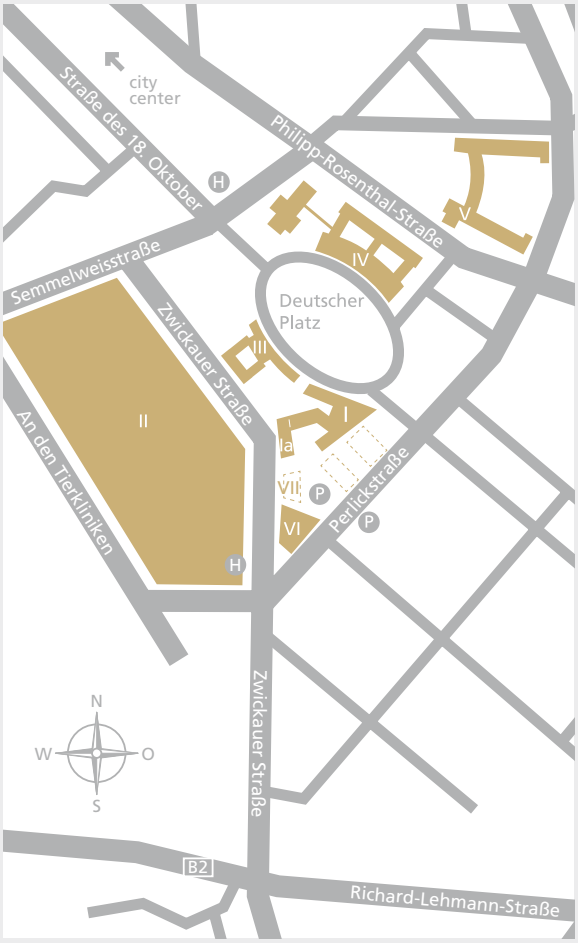
Numerous partners in the immediate vicinity

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). Institutions relevant for cooperation are, above all, 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. Therefore, also in 2011, the Fraunhofer IZI organized and supported various publicity event formats, at the same time presenting itself and its subject areas

Topping out ceremony for the extension building

When the institute building was officially opened, the officiating Federal Minister of Transport at the time and former mayor of Leipzig, Wolfgang Tiefensee, wished the Fraunhofer IZI a speedy cell division. This symbolic cell division is now clearly visible, as on February 2, 2011 the first extension building's shell was completed. A close circle of colleagues and construction workers celebrated the topping out ceremony. By the end of the year, work on the façade was completed. The interior construction is also coming on in leaps and bounds. The building is expected to be handed over and put into operation in the middle of 2012.

The "daughter cell" is situated directly next to the main building and will contain modern research laboratories, offices and a further clean room facility, all over a total area of 3 280 m². In future, the laboratories are primarily intended for regeneration research and therapy development. Modern equipment including various imaging technologies will complete the institute's service portfolio and capacities. The clean room capacities will be extended by around 450 m² with the new construction. This means that in future, cell therapy preparations for clinical trials can be manufactured at the Fraunhofer IZI over a 900 m² area.

The overall costs of the extension building amount to around 8.6 million euros and are being financed with funds provided by the EU, the federal government, and the Free State of Saxony.

10 years of the Fraunhofer Group for Life Sciences

The institutes of the Fraunhofer-Gesellschaft cooperate in groups to pool different competencies, thus facilitating the development of complex system solutions and integrated innovations. For ten years now, the competencies of life sciences have been consolidated into the Fraunhofer Group for Life Sciences. By networking within the Fraunhofer-Gesellschaft, natural sciences and engineering have crossed paths and synergies have been created. Investigating health issues is one of the group's most pressing tasks. On March 31, 2011, in celebration of its tenth anniversary, the group invited institute representatives and guests from the fields of economy and politics to Berlin to celebrate joint achievements and discuss future challenges. Current and future tasks and markets were debated in keynote speeches and podium discussions. In an accompanying exhibition, the group's institutes – including the Fraunhofer IZI – presented a range of projects and developments.

"Research and discover!" is Saxony's motto in its bid to become a research metropolis

Under the motto "Research and discover!", Saxony's State Ministry for Science and the Arts invited entrepreneurs, researchers and interested guests to an information event in Leipzig on May 23, 2011. "In Saxony, we have the potential and the sheer will to become one of the economically and scientifically leading regions in Europe by 2020," said State Minister Professor Sabine von Schorlemer when summarising the purpose of the event in her invitation. Around 300 attendees followed the call to the KUBUS at the Helmholtz Centre for Environmental Research (UFZ). In various keynote speeches and a podium discussion, the significance of research being carried out at universities and non-university research facilities for the region's economic development was emphasized and the potential of the transfer of humanistic insights into the economy and society was discussed. The Fraunhofer IZI helped coordinators organise the event and used the accompanying technical exhibition to present themselves to their attentive audience.

Day of mobility and technology

Over the past few years, the former trade fair grounds in the south east of Leipzig have become a dynamically growing economic and scientific sector. When the Fraunhofer IZI was founded in 2005, a conscious decision was made to settle at this location in close proximity to BIO CITY, the university hospitals and other research facilities. By means of regular events, members of the "Alte Messe" syndicate present themselves to the public and demonstrate their activities and achievements. This was also the case on October 8, 2011: under the motto "mobility and technology", local companies and institutions showcased exciting subjects from the fields of culture, economy and science. Visitors were assured of the dynamic development of the site through a series of lectures, information stands and hands-on activities. The Fraunhofer IZI introduced itself by means of an information booth and also gave insights into modern medical research through a talk given by the Stem Cell Biology Unit.

Fraunhofer Life Science Symposium

As part of the "World Conference on Regenerative Medicine", the "Fraunhofer Life Science Symposium" (FSL) took place on November 3, 2011 at the Congress Center in Leipzig. This year the overriding theme was that of innovative biomaterials and biological 3D scaffolds. The event was organized by the Fraunhofer IZI as well as the Fraunhofer Institute for Mechanics of Materials and the Fraunhofer Additive Manufacturing Alliance. On November 29–30, 2012, the annual event will be hosted in cooperation with the German Society for Stem Cell Research (Deutsche Gesellschaft für Stammzellforschung e.V., GSV). New findings from the field of stem cell research will then be presented at the Fraunhofer IZI, with particular emphasis on clinical applications.

Movie talk: "My Sister's Keeper"

Scientific advancement within the area of stem cell research and cell therapy raises various issues and controversies among the general public. On November 10, 2011, as part of the Movie Talk event, interested attendees had the opportunity to discuss the topic of "saviour siblings" with experts from the fields of research, clinical medicine and law. This discussion was stimulated by the film "My Sister's Keeper". The protagonist of the film, which was released in Germany in August 2009, is the twelve-year-old Anna, who is conceived as a "saviour sibling" for her older sister Kate who is suffering from leukaemia. Even as a young child, Anna is made to undergo various procedures, for example to donate bone marrow, in order to save her sister's life. When the time comes for her to also donate a kidney, Anna wins her court case to have independence and freedom of choice with regards to her own body. The film therefore not only poses a number of medical issues, but also ethical controversies. What options does modern medicine really offer and which can be used in the knowledge that they are ethically justifiable? How far are people allowed to go to save lives? Discussing and debating these and other issues was the aim of the event, which was conjunctively organized by the German Society for Regenerative Medicine, the Fraunhofer IZI and the Forum of Contemporary History Leipzig. Around 150 attendees took advantage of the opportunity to learn more about this subject matter, both emotionally and factually.

The German Association of Research-based Pharmaceutical Companies discusses Saxony's future in research and development

On October 26, 2011, the German Association of Research-based Pharmaceutical Companies held an open forum at the Fraunhofer IZI on the topic "From research and location policy to network policy". The fact that Saxony is a first-class research location was quickly agreed upon by members of the forum. With its status, Saxony aims to act as a role model, both for Germany and Europe, for enhancing research applications. At the Lisbon Agenda in 2000, it was agreed for Europe that three percent of the gross domestic product should be spent on making Europe the most competitive research area in the world. At 2.68 percent, Saxony is on the right path, commented Saxony's Minister of Science, Professor Sabine von Schorlemer, in a key note speech.

In order to achieve these goals, close collaboration is required, above all, between politics, science and economy. High-ranking representatives from these sectors therefore used this evening to discuss framework conditions and strategies to boost the locations of both Saxony and Germany to become more globally competitive. Topics such as the transfer of state-funded research projects into market-ready products, as well as setting up businesses originating from universities and research facilities, were at the forefront of the discussion. Around 150 guests attended the event and joined in the forum with lively exchanges.

12th Pupils' Conference "Studies and Careers"

Thanks to its interesting architecture and communicative, light ambience, the Fraunhofer IZI is a popular location for holding events for a wide range of occasions. With this in mind, the Rotary Club of Leipzig-Brühl, the Protestant School Centre, and the St. Thomas School Leipzig all came together to organise the 12th pupils' conference "Studies and Careers" at the Fraunhofer IZI on December 2, 2011. In line with the charitable objectives of the Rotary Foundation with regards to promoting vocational education, the pupils' conference aims to empower young people to make good decisions when it comes to their future career paths. The Fraunhofer IZI shares this aspiration and was therefore also happy to offer its support. Around 250 pupils took the opportunity to not only find out about the institute, but to also learn more about the various professional fields. Over the course of a day, more than 60 speakers gave insights into their jobs, shared their experiences and took questions from pupils. This does not mean that the decision could be taken out of the pupils' hands; with newly gained impressions and information, however, an initial foundation paving the way to a future career was certainly created.

LOOKING TO 2012

The Fraunhofer IZI will continue to organize and hold various exciting events in 2012.

June 29, 2012 – Long Night of the Sciences

For the third time now, Leipzig's science and research institutions will open their doors long into the night. With a colourful programme consisting of guided tours, activities, talks and demonstrations, the institutions will stage research topics and projects to visitors.
www.wissenschaftsnacht-leipzig.de

May 2–5, 2012 – "7th International Symposium on Neuroprotection and Neurorepair"

The symposium addresses scientists and clinicians from the field of neurology sciences. Due to the broad diversity of subjects, the event sees itself as a platform for exchanging knowledge, particularly in the field of neurodegeneration and neuroregeneration. The symposium is being organized by the Cell Therapy Department and will take place in Potsdam this year.
www.neurorepair-2012.de

November 1–2, 2012 – Fraunhofer Innovation Forum 2012 Demography + Health Resources "Individuality. Vitality. Quality."

The Fraunhofer Innovation Forum "Health and Demography" brings together experts from the fields of health management, politics and research. Innovations stemming from medicine and health sciences are at the focus of the forum, as well as their influence on company and life practice. The event is being organized by the European Association for Vitality and Active Ageing (Europäische Vereinigung für Vitalität und Aktives Altern e. V.) together with the German Association for Health Related Fitness and Sport Therapy, and the Fraunhofer IZI.
www.age-plus-health.eu

November 7–10, 2012 – "International Meeting of the German Society for Cell Biology – molecular concepts in epithelial differentiation, pathogenesis and repair"

This event is being organized by the German Society for Cell Biology and will take place at the beginning of November at the Fraunhofer IZI.
www.zellbiologie.de

November 29–30, 2012 – 7th "Fraunhofer Life Science Symposium" Leipzig and 7th Annual Congress of the German Society for Stem Cell Research

The seventh "Fraunhofer Life Science Symposium" is associated with the annual conference of the German Society for Stem Cell Research. Researchers and physicians will debate the areas "stem cells and clinical applications" and discuss the most recent findings.
www.fs-leipzig.com

SCIENTIFIC PRESENCE

CONVENTIONS AND CONFERENCES

- **1st Innovation Conference Medical Saxony** (attendee), August 30, 2011, Leipzig, Germany
- **10th Research Festival Leipzig 2011** (poster), December 16, 2011, Leipzig, Germany
- **12th Young Scientist Meeting of the German Society for Cell Biology (DGZ) "RNA and Disease"** (poster / oral presentation), September 8–10, 2011, Jena, Germany
- **2011 BIO International Convention** (attendee), June 27–30, 2011, Washington, USA
- **2011 Joint Annual Meeting SIICA and DGfI** (poster), September 28–October 1, 2011, Riccione, Italy
- **3rd Symposium "Urological Research" of the German Society of Urology** (oral presentation), November 17–19, 2011, Jena, Germany
- **7th Düsseldorf Symposium on Immunotoxicology "Biology of the Aryl Hydrocarbon Receptor"** (poster), September 21–24, 2011, Düsseldorf, Germany
- **Advanced vocational training meeting of the department for internal medicine of the University Hospital Leipzig** (oral presentation), February 1 / May 31 / October 25, 2011, Leipzig, Germany
- **Annual Meeting of the German Association for the Fight Against Virus Diseases** (oral presentation), September 29–30, 2011, Leipzig, Germany
- **Annual Meeting of the DGfI Working Group for Veterinary Imunology** (poster), November 11–12, 2011, Munich, Germany
- **Annual Meeting of the German Society for Biomedical Engineering** (oral presentation), September 27–30, 2011, Freiburg, Germany
- **Annual Meeting of the German Society for Cytometry** (oral presentation), October 12–14, 2011, Bonn, Germany
- **Annual Meeting of the German Society for Gerontology** (poster), December 2–3, 2011, Ulm, Germany
- **Annual Meeting of the German Society for Immunology** (poster), September 28–October 1, 2011, Riccione, Italy
- **Annual Meeting of the German Society for Zoology** (oral presentation), September 9–12, 2011, Saarbrücken, Germany
- **Annual Meeting of the Working Group of the Institutes for Bee Research** (oral presentation), March 29–31, 2011, Berlin, Germany
- **Annual Scientific Meeting of the British Society for Research on Ageing** (oral presentation), July 11–14, 2011, Brighton, UK
- **BIO-Europe** (attendee), October 31–November 2, 2011, Düsseldorf, Germany
- **BIT's 4th Annual World Congress of Regenerative Medicine & Stem Cell** (oral presentation), November 11–13, 2011, Peking, China
- **Cell Culture World Congress 2011** (attendee), February 28–March 2, 2011, Munich, Germany
- **Charité Entrepreneurship Summit 2011** (attendee), April 11–12, 2011, Berlin, Germany
- **EMBO Conference Series "Chromatin and Epigenetics"** (poster), June 1–5, 2011, Heidelberg, Germany
- **Entomologist Meeting 2011** (oral presentation), March 21–24, 2011, Berlin
- **European Antibody Congress 2011** (attendee), November 29–December 1, 2011, Geneva, Switzerland
- **European Lab Automation. Advances in Biodetection and Biosensors** (poster), June 30–July 1, 2011, Hamburg, Germany
- **European Society for Clinical Cell Analysis 2011 Conference** (poster), September 13–17, 2011, Dublin, Irland
- **EuroWestNile Meeting** (oral presentation), October 7, 2011, Madrid, Spain
- **German Biotechnology Days 2011** (attendee), May 25–26, 2011, Munich, Germany
- **German Korean Symposium** (oral presentation), March 2–6, 2011, Gwanju / Hwasun, Korea
- **International Meeting "Emerging Vector-Borne Viral Diseases"** (oral presentation), September 9, 2011, Padua, Italy
- **Islet Transplantation Symposium** (oral presentation), Leuven, Belgium
- **Joint Annual Meeting of the German and Austrian Society for Hematology and Oncology, the Swiss Society for medical Oncology, and the Swiss Society for Hematology** (oral presentation), October 4, 2011, Basel, Switzerland
- **LIFE – Science Day** (poster), November 29–30, 2011, Leipzig, Germany
- **Medica 2011** (attendee), November 16–19, 2011, Düsseldorf, Germany
- **Meeting of the Korean Society for Ageing Research** (oral presentation), Pusan, Korea
- **Meeting of the National Association of Saxon Beekeepers** (oral presentation), February 9, 2011, Leipzig, Germany
- **MicroSystemEngineering Congress 2011** (oral presentation), October 10–12, 2011, Darmstadt, Germany
- **National Symposium on Zoonoses Research 2011** (poster), October 6–7, 2011, Berlin, Germany
- **Prevention and Intervention: From Molecular Biology to Clinical Perspectives; Interdisciplinary Centre on Ageing in Halle (IZAH)** (poster / attendee), September 16–18, 2011, Halle, Germany
- **Rostock Symposium on Systems Biology and Bioinformatics in Ageing Research** (oral presentation), September 15–17, 2011, Rostock, Germany
- **Structure- & Computer-Aided Design Workshop: Bioactive Molecules & Materials** (oral presentation), November 7–11, 2011, Athens, Greece
- **World Conference on Regenerative Medicine** (oral presentation / poster attendee / chair), November 2–4, 2011, Leipzig, Germany
- **World Immune Regulation Meeting V** (poster), March 24–27, 2011, Davos, Switzerland

RESEARCH PARTNERS

- **AIT Austrian Institute of Technology GmbH,** Department of Heath and Environment, Vienna, Austria
- **Association CARDIO-MONDE,** Laboratory of Biosurgical Research, Paris, France
- **Biomedical Primate Research Centre,** Department of Virology, Rijswijk, The Netherlands
- **Charité – Universitätsmedizin Berlin,** Berlin, Germany

- **Clinic St. Georg gGmbH,** Robert Koch Clinic, Leipzig, Germany
- **Deutsches Herzzentrum Berlin (DHZB, German Heart Institute Berlin),** Laboratory for Tissue Engineering, Berlin, Germany
- **Ernst Moritz Arndt University Greifswald,** Faculty of Medicine, Clinic and Polyclinic for Neurology, Greifswald, Germany
- **Flensburg University of Applied Sciences,** Department of Engineering, Flensburg, Germany
- **Fraunhofer Applications Center for Processing Machinery and Packaging Technology AVV,** Dresden, Germany
- **Fraunhofer Institute for Biomedical Engineering IBMT |** Division of Ultrasound, Biomedical Applications and Imaging Unit, St. Ingbert, Germany
- **Fraunhofer Institute for Electron Beam and Plasma Technology FEP** | Biomedical Laboratory Unit, Dresden, Germany
- **Fraunhofer Institute for Manufacturing Technology and Advanced Materials IFAM,** Bremen, Germany
- **Fraunhofer Institute for Mechanics of Materials IWM,** Business Unit Biological and Macromolecular Materials, Halle / Saale, Germany
- **Fraunhofer Institute for Nondestructive Testing IZFP,** Business Unit Environment, Energy, Life Sciences, Dresden, Germany
- **Fraunhofer Institute for Process Engineering and Packaging IVV,** Business Unit Food Quality and Sensory Acceptance, Munich | Business Unit Processing and Packaging Machinery, Dresden, Germany
- **Fraunhofer Institute for Reliability and Microintegration IZM,** Berlin, Germany
- **Fraunhofer Institute for Toxicology and Experimental Medicine ITEM** | Research Area Airway Research, Biomarkers and Infection Unit, Hanover, Germany
- **Freie Universität Berlin (Free University of Berlin),** Department of Veterinary Medicine, Berlin, Germany
- **Friedrich Loeffler Institute, Federal Research Institute for Animal Health,** Institute for Novel and Emerging Infectious Diseases (INNT), Greifswald, Germany
- **Helmholtz Center for Environmetal Research UFZ,** Department Environmental Microbiology | Department Proteomics | Department Environmental Immunology, Leipzig, Germany
- **Herzzentrum Leipzig GmbH (Heart Center Leipzig),** Clinic for Cardiology, Leipzig, Germany
- **Institut de Recerca de l'Hospital Santa Creu i Sant Pau,** Barcelona, Spain
- **Institut Quimíc de Sarrià, Fundació Privada,** Barcelona, Spain
- **Leibniz Institute for Neurobiology (LIN),** Research Group Neuropharmacology, Magdeburg, Germany
- **Leibniz Institute of Surface Modification,** Research Area Ultra-Precise Surface Finishing, Leipzig, Germany
- **Ludwig Maximilians University Munich,** Faculty of Veterinary Medicine, Munich, Germany
- **Martin Luther University Halle-Wittenberg,** Faculty for Natural Sciences I – Biosciences, Institute for Biology, Halle / Saale, Germany
- **McGill University,** Faculty of Medicine, Cognitive Neuroscience Unit, Montreal, Canada
- **Oslo University Hospital Radiumhospitalet,** Division of Cancer Medicine, Surgery & Transplantation, Institute for Cancer Research, Oslo, Norway
- **Polish Academy of Sciences,** Centre for Molecular and Macromolecular Studies, Department of Engineering of Polymer Materials, Łódź, Poland
- **Radboud University Nijmegen Medical Centre,** Department of Urology, Experimental Urology, Nijmegen, The Netherlands
- **Research Center Borstel – Leibniz Center for Medicine and Biosciences,** Borstel, Germany
- **Saxon State Office for Environemt, Agriculture, and Geology,** Dresden, Germany
- **Seoul National University,** Government-funded Research Centers, Nano Systems Institute, Seoul, Korea
- **Southern Medical University China,** South Genomics Research Center, Guangzhou, China
- **St. Elisabeth Clinic Leipzig, Academic Teaching Hospital of the University of Leipzig,** Deparmtent for Urology | Breast Center, Leipzig, Germany
- **Technical University Munich,** Faculty for Medicine, Institute for Radiology, Department for Neuroradiology, Munich, Germany
- **The Hebrew University – Hadassah Medical School,** Lautenberg Center for General and Tumor Immunology, Jerusalem, Israel
- **The Hebrew University of Jerusalem,** School of Pharmacy, Neuropharmacology and Neurotoxicology Laboratory, Jerusalem, Israel
- **Universidad Politécnica de Valencia,** Center for Biomaterials, Valencia, Spain
- **Università degli Studi di Padova,** Padova, Italy
- **Université d'Evry Val-d'Essonne,** INSERM UMR861/UEVE/CECS, Evry cedex, France
- **Universiteit Ghent,** Faculty of Veterinary Sciences, Laboratory for Gene Therapy, Ghent, Belgium
- **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 | Depart-

ment for Diagnostics, Institute for Clinical Immunology and Transfusion Medicine | Department for Diagnostics, Institute for Medical Mikrobiology and Infection Epidemiology | Department for Diagnostics, Institute for Pathology | Department for Diagnostics, Institute for Virology | Department for Internal Medicine, Neurology and Dermatology, Clinic and Polyclinic for Gastroenterology and Rheumatology | Department for Internal Medicine, Neurology and Dermatology, Division for Hematology and Internal Oncology | Clinic and Polyclinic for Ophthalmology, Leipzig, Germany

- **University Clinic Münster,** Clinic and Polyclinic for Neurology, Münster, Germany
- **University Clinic Regensburg,** Institute for Immunology, Regensburg, Germany
- **University Clinic Rostock,** Clinic and Polyclinic for Radiation Therapy, Rostock, Germany
- **University of Cologne,** Faculty of Mathematics and Natural Sciences, Department for Chemistry, Institute of Biochemistry, Cologne, Germany
- **University of Leipzig,** Center for Biotechnology and Biomedicine | Faculty for Biosciences, Pharmacy and Psychology | Institute for Informatics, Professorship for Bioinformatics | Faculty of Medicine | Faculty of Medicine, Medical Experimental Center | Translational Center for Regenerative Medicine | Translational Center for Regenerative Medicine, Microsurgery and Animal Models Core Unit (MACU) | Faculty for Veterinary Medicine | 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, Medical Animal Clinic | Faculty for Veterinary Medicine, Institute for Veterinary Anatomy | Faculty of Medicine, Institute for Medical Informatics, Statistics und Epidemiology (IMISE), Leipzig, Germany
- **University of Liverpool,** Liverpool, UK
- **University of Massachusetts,** School of Medicine, Neurology Department, Worcester, USA
- **University of Regensburg,** Faculty for Medicine, Regensburg, Germany
- **University of Rostock,** Faculty for Medicine, Clinic for Internal Medicin, Rostock, Germany
- **University of Salzburg,** Priority Programme BioScience and Health, Salzburg, Austria
- **University of Würzburg,** Institute for Virology and Immunobiology, Würzburg, Germany
- **University of Zurich,** Vetsuisse Faculty, Institute for Laboratory Animals, Zurich, Switzerland
- **Urological Practice & Study Institute Dr. Schulze,** Markkleeberg, Germany
- **Washington University,** School of Medicine, Division of Infectious Diseases, St. Louis, USA

ADVANCED VOCATIONAL TRAINING

- **3rd Leipzig Myeloma Meeting,** University Clinic Leipzig, Leipzig, Germany
- **3rd Autumn School "Current Concepts in Immunology",** German Society for Immunology (DGfI), Bad Schandau, Germany
- **7th Spring School on Immunology,** German Society for Immunology (DGfI), Ettal, Germany
- **8th Oncological Summer Symposium,** University Clinic Leipzig, Leipzig, Germany
- **Advanced Therapies (ATMPs),** University of Leipzig, Translational Center for Regenerative Medicine TRM, Leipzig, Germany
- **Animal experimentation course,** University of Leipzig, Faculty for Medicine, Medical Experimental Center, Leipzig, Germany
- **Application and blood sampling techniques on mice and rats,** Charles River, Research Models and Services, Germany GmbH, Essen, Germany
- **ATMP and tissue – quality and safety requirements,** Concept Heidelberg GmbH, Mannheim, Germany
- **Coagulation symposium,** University Clinic Leipzig, Leipzig, Germany
- **English course,** LSI World of Languages GmbH, Leipzig, Germany
- **First aid course,** Fraunhofer IZI, Leipzig, Germany
- **Foundation course in the study of laboratory animals,** University of Leipzig, Faculty for Medicine, Medical Experimental Center, Leipzig, Germany
- **Fraunhofer mentoring programme,** Fraunhofer-Gesellschaft, Munich / Leipzig / Stuttgart, Germany
- **German Medical Devices Legislation (Medizinprodukterecht),** University of Leipzig, Translational Center for Regenerative Medicine, Leipzig, Germany
- **Good Manufacturing Practice (GMP),** University of Leipzig, Translational Center for Regenerative Medicine, Leipzig, Germany
- **Hazardous materials training for infectious materials, category B biological substances and dry ice,** World Courier (Deutschland) GmbH, Berlin, Germany
- **Immunohistology course,** Histoconsulting, Leipzig, Germany

- **Medical specialist training: internal medicine / gastro-enterology / haematology / oncology / haemostaseology,** University Clinic Leipzig, Leipzig, Gemany
- **MultiColor flow cytometry for the characterization of stem cells,** Becton Dickinson GmbH, Heidelberg, Germany
- **OSHO autumn convention on haematology / oncology / haemostaseology,** University Clinic Leipzig, Zwickau, Germany
- **OSHO spring convention on haematology / oncology / haemostaseology,** University Clinic Leipzig, Leipzig. Germany
- **Project Management,** University of Nottingham, Institute of Leadership and Management, Nottingham, UK
- **QA 14 – GMP- / manufacturing and testing of clinical investigational drugs in line with the FDA,** Concept Heidelberg GmbH, Mannheim, Germany
- **QM foundation course for laboratory assistants,** Dr. Klinkner & Partner GmbH, Potsdam, Germany
- **Quality assurance in the cell culture laboratory,** Institute for Molecular Bbiology, Research-Diagnostics-Education, Prof. Dr. Gerhard Unteregger, Homburg / Saar, Germany
- **Quality control management,** Concept Heidelberg GmbH, Mannheim, Germany
- **Quality management for laboratory assistants,** Dr. Klinkner & Partner GmbH, Potsdam, Germany
- **Quality specialists,** TÜV Academy, Berlin, Germany
- **Reimbursement of costs for ATMPs and medical devices,** University of Leipzig, Translational Center for Regenerative Medicine, Leipzig, Germany
- **Responsible implementation and integrative challenge of quality assurance,** World Courier (Deutschland) GmbH, Leipzig, Germany
- **University professor training,** University of Leipzig, Leipzig, Germany
- **Zoology,** University of Leipzig, Leipzig, Germany

TEACHING ACTIVITIES

- **University of Leipzig:**
  - Acute leukaemia (course)
  - Additional training qualification for out-of-work academics to integrate into the biotechnology sector (practical training)
  - Animal models in research (lecture)
  - Basics of immunology (lecture)
  - Hybridoma cell culture techniques for manufacturing monoclonal antibodies (lecture)
  - Immunological methods (lecture)
  - Immunological practical training for medical practitioners (practical training)
  - Infectiology and immunology (problem-oriented learning)
  - Introduction to clinical medicine (course)
  - Lymphomas (course)
  - New technologies in the development of vaccines (lecture)
  - QSB seminar on environmental medicine disease patterns in adults (seminar)
  - QSB, tissue typing (seminar)
  - QSB4 transfusion medicine (seminar)
  - Regenerative medicine (lecture)

EVALUATOR ACTIVITIES

- **Bioinformatics,** Dr. Jörg Hackermüller
- **BMC Bioinformatics,** Dr. Jörg Hackermüller
- **Brain Research,** Dr. Daniel-Christoph Wagner
- **Experimental Neurology,** Dr. Daniel-Christoph Wagner
- **Future Drugs – Expert Reviews Vaccines,** Dr. Jörg Lehmann
- **German Research Foundation,** Dr. Jörg Hackermüller
- **Interreg** (Community Initiative of the European Regional Development Fund), Dr. Dirk Kuhlmeier
- **Intervirology,** Dr. Sebastian Ulbert
- **Journal of Antivirals & Antiretrovirals,** Dr. Sebastian Ulbert
- **Journal of Controlled Release,** Dr. Sebastian Ulbert
- **Journal of Neuroscience Research,** Dr. Daniel-Christoph Wagner
- **Molecular Oncology,** Dr. Kristin Reiche
- **Neurobiology of Disease,** Dr. Daniel-Christoph Wagner
- **Recent Patents on Regenerative Medicine,** Dr. Daniel-Christoph Wagner
- **Research Foundation – Flanders, FWO,** Dr. Daniel-Christoph Wagner
- **The Open Veterinary Science Journal** (Editorial Board), Dr. Jörg Lehmann
- **Vaccine,** Dr. Sebastian Ulbert
- **Veterinary Immunology and Immunopathology,** Dr. Jörg Lehmann
- **Virus Research,** Dr. Sebastian Ulbert

- **World Conference on Regenerative Medicine** (abstact evaluation / chair), Dr. Myriam Peters, Dr. Stephan Fricke, Dr. Jörg Lehmann, Alexander Kranz, Dr. Daniel-Christoph Wagner, Dr. Alexandra Stolzing, Dr. Dirk Kuhlmeier, Prof. Dr. Ulrich Sack, Dr. Dr. Johannes Boltze

ASSOCIATION MEMBERSHIPS

- **American Heart Association,** Dr. Alexander Deten
- **Association for Cancer Immunotherapy (CIMT),** Christopher Oelkrug M.Sc.
- **Association for the Advancement of Immune Diagnostics,** Prof. Dr. Ulrich Sack (executive board)
- **Biosaxony e.V.,** Dr. Thomas Tradler
- **Biotechnology Network Berlin-Brandenburg e.V.,** Dr. Thomas Tradler
- **Cental Committee for Animal Protection, Directorate Leipzig,** Dr. Jörg Lehmann
- **European Autoimmunity Standardization Initiative (EASI),** Prof. Dr. Ulrich Sack (Vorstand)
- **European Molecular Biology Laboratory (EMBL) Alumni Association,** Dr. Sebastian Ulbert
- **European Society for Clinical Cell Analysis (ESCCA),** Prof. Dr. Ulrich Sack (Vorstand)
- **European WNV Research Platform,** Dr. Sebastian Ulbert
- **Friends of Veterinary Medicine Faculty of the University of Leipzig,** Dr. Jörg Lehmann
- **German Association of University Professors and Lecturers,** Dr. Alexander Deten
- **GDCh (German Chemical Society),** Dr. Michael Szardenings
- **German Society for Cardiology – Cardiovascular Research,** Dr. Alexander Deten
- **German Society for Clinical Chemistry and Laboratory Medicine,** Prof. Dr. Ulrich Sack
- **German Society for Gerontology,** Dr. Alexandra Stolzing
- **German Society for Gerontology and Geriatrics,** Dr. Alexandra Stolzing (deputy head of section)
- **German Society for Immunology,** Christiane Füldner, Christopher Oelkrug M.Sc., Dr. Jens Knauer, Dr. Jörg Lehmann, Dr. Stephan Fricke, Franziska Lange, Prof. Dr. Ulrich Sack (delegate)
- **German Society for Regenerative Medicine,** Dr. Alexandra Stolzing (member of the committee), Dr. Stephan Fricke
- **German Society for Virology,** Dr. Sebastian Ulbert
- **German Society for Zoology,** Gustavo Makert dos Santos
- **German Society of Physiology,** Dr. Alexander Deten
- **GLP Commission,** Prof. Dr. Ulrich Sack (executive board)
- **International Behavioural and Neural Genetics Society (IBANGS),** Dr. Holger Kirsten
- **International Society for Heart Research (ISHR),** Dr. Alexander Deten
- **International Union for the Study of Social Insects,** Gustavo Makert dos Santos
- **National Research Platform for Zoonoses,** Dr. Sebastian Ulbert
- **GBM (German Society for Biochemistry and Molecular Biology),** Dr. Michael Szardenings
- **Society for Laboratoy Animals (GV-SOLAS),** Dr. Jörg Lehmann
- **Society for Neuroscience (SfN),** Björn Nitzsche, Dr. Daniel-Christoph Wagner, Teresa von Geymüller, Vilia Zeisig
- **Study-group for Experimental Stem Cell Transplantation,** Dr. Stephan Fricke
- **The RNA Society,** Dr. Jörg Hackermüller

PRIZES

- **2nd poster prize at the "7th Düsseldorf Symposium on Immunotoxicology – Biology of the Aryl Hydrocarbon Receptor"** (September 21–24, 2011) of the Leibnitz Research Institute for Environmental Medicine for Christiane Füldner, Dr Jens Knauer and Dr Jörg Lehmann from the Cell Engineering / GLP Unit on the topic of "Immunomodulatory effects of Benzo(a)pyrene influencing the outcome of infection with Salmonella enterica".
- **Fulbright grant** of the German-American Fulbright Commission for Marianna Sofman from the Nanotechnology Unit on the topic "Functionalized nanoparticles".
- **Prize awarded by the Working Group for Urological Research (Medicine)** of the German Society of Urology for Rudi Ascherl and Kerstin Boll from the RNomics Unit on the topic "Three microRNAs down-regulated in prostate carcinoma suppress synergistic, central oncogenic signalling pathways".
- **Prize for winning the largest industry new client project in the first quarter of 2011** of the Fraunhofer-Gesellschaft for Kati Kebbel, Anja Fanselow and Gerno Schmiedeknecht from the Cell Engineering / GMP Unit for a project with Cognate BioServices Inc.

PUBLICATIONS

JOURNAL ARTICLES

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GRADUATION

- Allelein, Susann. **Manufacturing of a zinc finger probe to be used in DNA-based diagnosis of staphylococcus aureus. (Herstellung einer Zink-Finger-Sonde zum Einsatz in DNA-basierter Staphylococcus aureus-Diagnostik.)** Friedrich-Schiller-Universität Jena, Diplom
- Bendull, Marcus. **Manufacturing of amylose and agarose 3D matrices to immobilise functional biomolecules. (Herstellung von Amylose und Agarose 3D-Matrizes zur Immobilisierung funktioneller Biomoleküle.)** Universität Leipzig, Bachelor
- Boltze, Johannes. **Neurobiological and clinical aspects of cell therapies for ischemic stroke – an interdisciplinary and translational study.** Universität Leipzig, Dissertation

- Ding, Huawen. **Dissecting the Wnt signaling pathway during osteogenic fate specification of embryonic stem cells.** Universität Leipzig, Dissertation
- Glocke, Isabelle. **Immunohistochemical differentiation of the astroglial reaction following an experimental stroke in rats. (Immunhistochemische Differenzierung der astroglialen Reaktion nach experimentellem Schlaganfall in der Ratte.)** Universität Leipzig, Bachelor
- Hennig, Katharina. **Generation and application of a DNA-binding protein. (Generierung und Applikation eines DNA-bindenden Proteins.)** Fachhochschule Jena, Bachelor
- Jaklin, Manuela. **The influence of astrocytes on neuroprotection following glucose and oxygen withdrawal. (Der Einfluss von Astrozyten auf die Neuroprotektion nach Glucose-Sauerstoff-Entzug.)** Universität Leipzig, Bachelor
- Kulpa, Konstanze. **Screening for Allergy Markers in Serum using Peptide Phage Display.** Universität Leipzig, Diplom
- Lorenzen, Maren. **Application of magnetic beads and biosensor systems in medical diagnostics. (Applikation magnetischer Beads und Biosensorsysteme in der medizinischen Diagnostik.)** Fachhochschule Flensburg, Bachelor
- Michalk, Stefanie. **Stereological quantification of secondary neuronal degeneration in the thalamus following an experimental stroke. (Stereologische Quantifizierung der sekundären neuronalen Degeneration im Thalamus nach experimentellem Schlaganfall.)** Universität Leipzig, Bachelor
- Poveda Zapata, Monica. **Development of a diagnostic platform for nucleic acids using an isothermal amplification.** Hochschule Bremerhaven / Universidad EAFIT, Medellin, Kolumbien, Bachelor
- Rothe, Katherina. **Influence of CD4+CD25+ regulatory T cells on haematopoietic reconstitution following syngeneic and allogeneic stem cell transplantation in a triple-fold transgenic mouse model. (Einfluss CD4+CD25+ regulatorischer T-Zellen auf die hämatopoetische Rekonstitution nach syngener und allogener Stammzelltransplantation in einem dreifach transgenen Mausmodell.)** Universität Leipzig, Dissertation
- Schneeweiss, Anne. **Development of a DNA vaccine using the example of the West Nile Virus. (Entwicklung eines DNA-Impfstoffs am Beispiel des West-Nil-Virus.)** Universität Leipzig, Dissertation
- Schneider, Marie. **The influence of benzo[a]pyrene on immunoglobuline production and cytokine expression in C57BL/6 mice. (Der Einfluss von Benzo[a]pyren auf die Immunglobulinproduktion und Zytokinexpression in C57BL/6-Mäusen.)** Universität Leipzig, Bachelor
- Trettner, Susanne. **Establishing a bioprocess for the osteogenic differentiation of embryonic stem cells of the common marmoset (Callithrix jacchus) in automated suspension bioreactors. (Etablierung eines Bioprozesses zur osteogenen Differenzierung von embryonalen Stammzellen des Weißbüschelaffens Callithrix jacchus in automatisierten Suspensionsbioreaktoren.)** Universität Leipzig, Dissertation
- Zeizinger, Steffen. **Antimicrobial peptide MUC7 (12-mer) – generation and characterisation of new effective mutants. (Antimikrobielles Peptid MUC7 (12-mer) – Generierung und Charakterisierung von neuen effektiven Mutanten.)** Martin-Luther-Universität Halle-Wittenberg, Diplom
- Zscheile, Caroline. **Imaging, anatomical and functional characterisation of focal cerebral ischaemia over time in sheep. (Bildgebende anatomische-funktionelle Charakterisierung der fokalen zerebralen Ischämie im Zeitverlauf am Schaf.)** Ernst-Moritz-Arndt-Universität Greifswald, Diplom

PATENTS

The Fraunhofer IZI currently holds 20 published and 10 granted patents (both inclusive of national variations) which are available for use in cooperation projects as well as for direct commercialization and licensing.

Furthermore, two additional patent registrations were submitted in the reporting year.

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FURTHERANCE

SPONSORS AND ADVISORY BOARD OF THE FRAUNHOFER IZI

The Fraunhofer IZI's successful development and continuous growth in the buildup phase was facilitated by the support and commitment of various institutions and persons.

Sponsors

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 throughout the current development phase.

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 are covered. The plot of land is provided by the City of Leipzig in hereditary leasehold and free of charge.

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Advisory board

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

Members of the advisory board:

- Dr. jur. Dr. h.c. oec. publ. Albrecht Schmidt (Chair) (Bayerische Hypo- und Vereinsbank AG, emeritus Chairman of the Supervisory Board)
- Dr. Knut Bartl (Roche Diagnostics GmbH, CSO Location Penzberg)
- Dr. Annerose Beck (Saxon State Ministry of Science and the Arts (SMWK), Deputy Head of National-Regional Research Centres Administration)
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- Prof. Dr. Hans-Martin Jäck (University Hospital Erlangen, Head of the Molecular Immunology Department)
- Prof. Dr. Friedrich-Wilhelm Mohr (Cardiac Center Leipzig GmbH – University Hospital – Medical Director)
- Prof. Dr. Gerhard Oechtering, University of Leipzig, Director of the Small Animal Hospital)
- Dr. med. Kai Pinkernell (Miltenyi Biotec GmbH, Head of Research in Clinical Development)
- Prof. Dr. med. Thomas Skutella (University of Heidelberg, Head of Department at the Institute for Anatomy and Cell Biology)

FRAUNHOFER-GESELLSCHAFT

THE FRAUNHOFER-GESELLSCHAFT IN PROFILE

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

At present, the Fraunhofer-Gesellschaft maintains more than 80 research units in Germany, including 60 Fraunhofer Institutes. The majority of the more than 20 000 staff are qualified scientists and engineers, who work with an annual research budget of €1.8 billion. Of this sum, more than €1.5 billion 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.

Affiliated international research centers and representative offices provide contact with the regions of greatest importance to present and future scientific progress and economic development.

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

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

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

Executive board (in December 2011)

Prof. Dr. Hans-Jörg Bullinger, President of the Fraunhofer-Gesellschaft, Corporate Management and Research
Prof. Dr. Ulrich Buller, Senior Vice President Research Planning
Prof. Dr. Alfred Gossner, Senior Vice President Finance and Controlling, IT
Dr. Alexander Kurz, Senior Vice President Personnel and Legal Affairs

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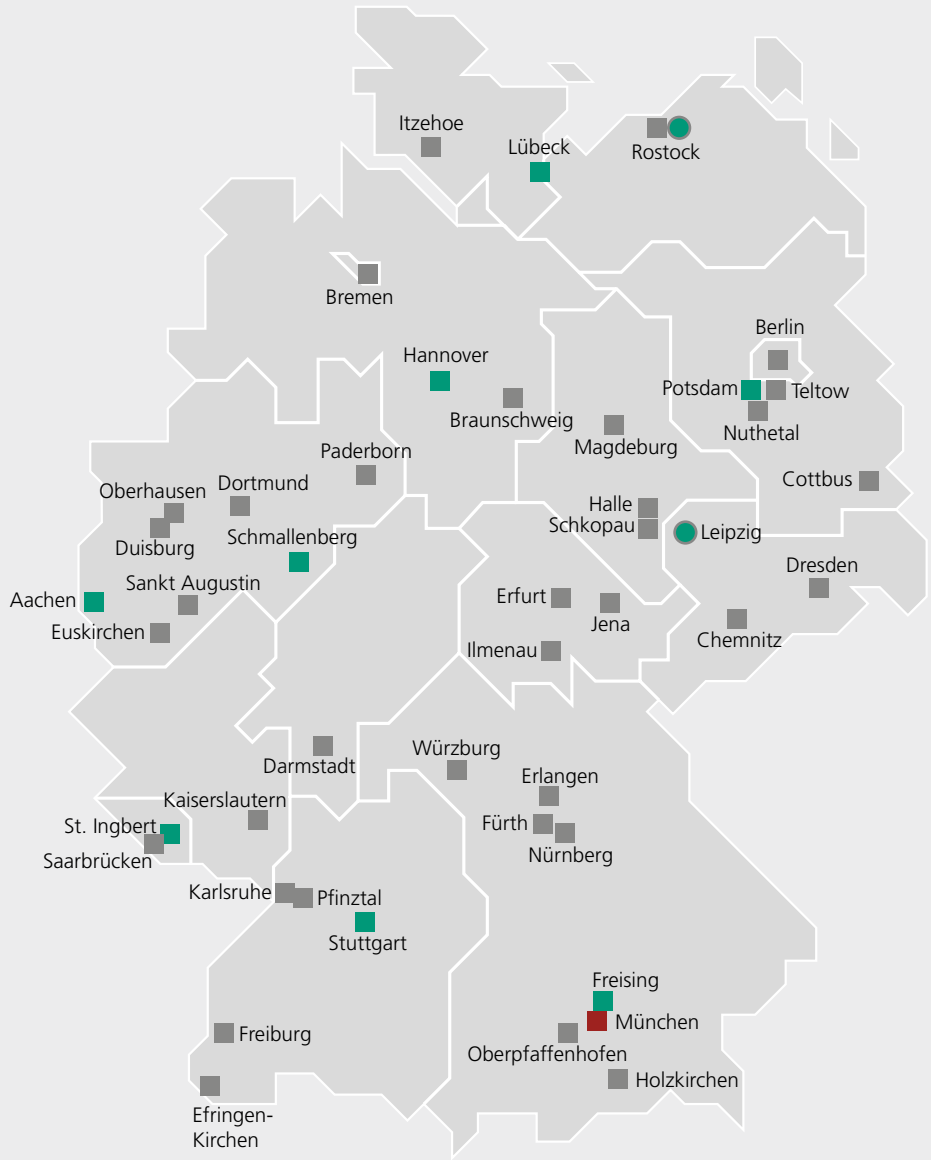
Locations



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

FRAUNHOFER GROUP FOR LIFE SCIENCES

To strengthen the biosciences, biomedicine and biotechnology, in 2001 the Fraunhofer Group for Life Sciences was created. It currently comprises six institutes.

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.

Business units of the Fraunhofer Group for Life Sciences:

- 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. Uwe Heinrich, who heads the Fraunhofer Institute for Toxicology and Experimental Medicine ITEM in Hanover. 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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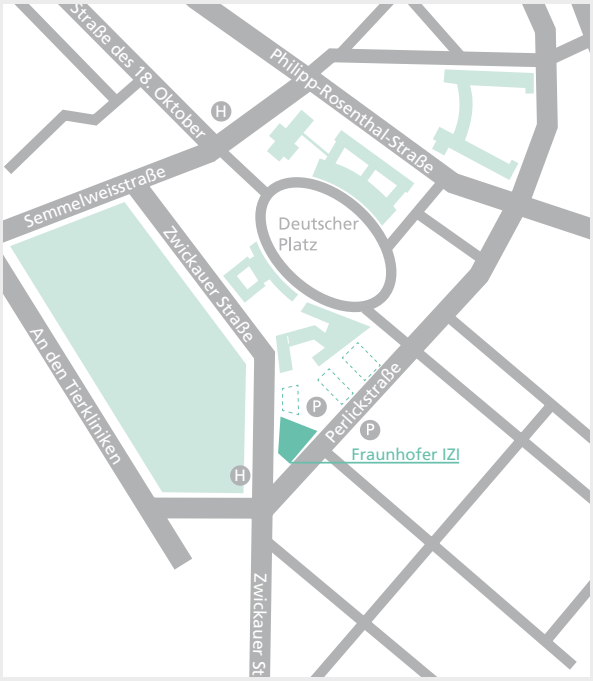

By car

Please note: Some navigation systems fail to find "Perlickstraße" as it is a private street belonging to the old trade fair grounds. We recommend that you enter "An den Tierkliniken" into your navigation system.

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 onto "Alte Messe" and after the second intersection turn right onto Puschstraße, at the end of which you turn left onto 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" and after the second intersection turn right into Puschstraße, at the end of which you turn left onto 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.

By train and public transport

Take the train to Leipzig Central Station ("Leipziger Hauptbahnhof"), then transfer to the number 16 tram in the direction of Lößnig and get off at the stop "An den Tierkliniken".

From the airport

From the airport take the urban train ("S-Bahn") to Leipzig Central Station ("Leipziger Hauptbahnhof"), then transfer to the number 16 tram in the direction of Lößnig and get off at the stop "An den Tierkliniken".

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INFORMATION SERVICE

Service Catalog

Our service catalog gives you a comprehensive insight into the products and services offered by the Fraunhofer IZI. On the basis of a sorting according to work units you will quickly find your appropriate contact person at our institute and gain insight into reference projects or applicabilities.

Annual Report

In combination with past years' issues, our current annual report gives you an insight into the structure of the Fraunhofer IZI, our services, important events and publications, offers, as well as selected project examples.

Homepage

An overview of interesting events held at the Fraunhofer IZI as well as further information on our institute can be found on our homepage www.izi.fraunhofer.de.

All our brochures and publications as well as current announcements made by the Fraunhofer IZI can be found on our homepage **www.izi.fraunhofer.de**. You can also mail to **presse@izi.fraunhofer.de** and order our brochures as hard copies.