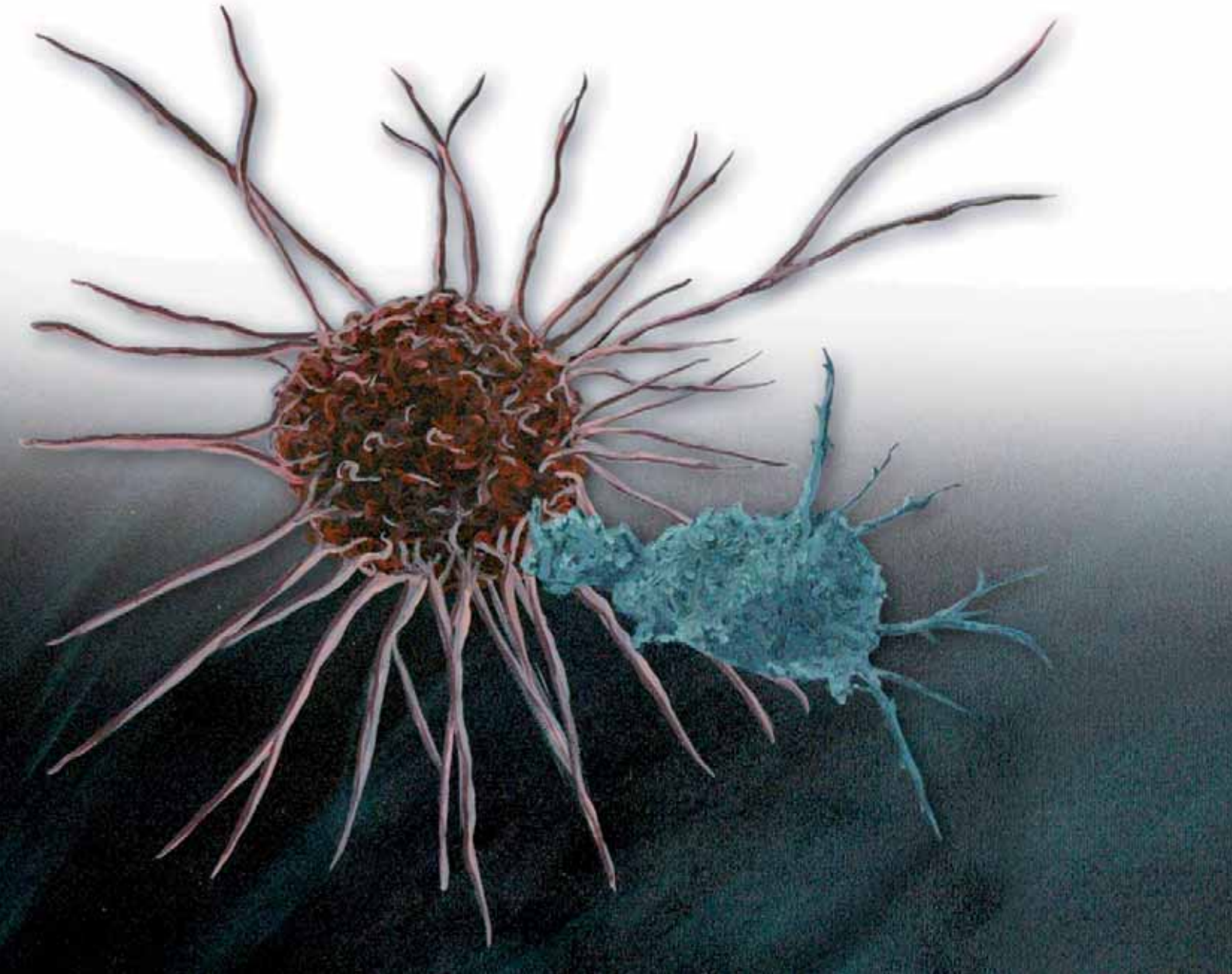
IZI

Fraunhofer Institut Zelltherapie und Immunologie

Annual Report 2007

www.izi.fraunhofer.de



Annual Report 2007

www.izi.fraunhofer.de

Contents

Dear Readers of our 2007 Annual Report,

A thrilling and busy year lies behind us. It was the second full business year for our young institute, the first Fraunhofer Institute in Leipzig. At the beginning of the year, we promised the advisory board and the executive board of the Fraunhofer-Gesellschaft to increase the project turnover to over 5 million euros in 2007, thereby doubling the turnover compared to 2006. We not only met this formidable goal, but exceeded it.

Our highly motivated young group leaders have succeeded in quickly establishing themselves a good reputation in the German research community. Their fundraising activities have resulted in many ambitious research and development contracts including three projects with a funding volume of over 1 million euros each. We are well positioned to build on such a solid foundation.

Internationally noticed scientific success was achieved by the RNomics Group with publications in the renowned journals "Nature" and "Science" on the significance of non-coded RNAs (nc-RNAs). In conjunction, we established an important and forward-looking technology platform that will help to develop new diagnostic and therapeutic procedures based on complex cellular steering mechanisms.

The Neurorepair Group succeeded in garnering the first research and development contract from a non-European organization for Fraunhofer IZI; the Cell Engineering/GMP Group favorably completed, together with our industry partner, the first successful audit through the "Regierungspräsidium Leipzig" and the federal authority in Frankfurt and received the license for the contracted production process. That this accomplishment followed so quickly after the rapid and smooth installation of the Fraunhofer IZI GMP facility for cell and tissue techniques is the best reference for the quality and performance potential of the institute.

In this report period, we established two new groups at Fraunhofer IZI. The Immunotherapy – Oncology Group, led by Dr. Christoph Schimmelpfennig, developed new cell therapies based on NK-cells and dendritic cells for the treatment of malignant tumors. Besides this development, the group offers new models for oncological therapy development. These models are based on the use of optical imaging techniques for the localization of tumor growth and cell migration.

The Cardiorepair Group, led by Dr. Alexander Deten, brings expertise on the precise determination of cardiological function and regenerative parameters to the institute. Cardiovascular disease remains, in industrialized nations, at the top of the morbidity and death statistics. Parallel to the Neurorepair Group, the Cardiorepair Group will develop and optimize cell therapeutic concepts for the treatment of tissues that have been damaged through oxygen deficiency. Its special therapy focus is heart attack.

The accomplishments of the institute were not only recognized and praised by the advisory board that has followed our steps with care, support and advice. In May 2007, the Fraunhofer IZI was visited by the Research Commissioner of the European Union, Dr. Potočnik, as well as the minister president of the Free State of Saxony, Prof. Milbradt. The most visible notice we received in 2007, however, was through leading the organization of the 3rd World Congress on Regenerative Medicine from October 18 - 20, 2007 in the Congress Center at the new Convention Center in Leipzig. A 30 percent increase in participant numbers and a doubling of industry participation lend credence to the increasing importance of regenerative medicine and the positive resonance of the event.

An ever-present discussion topic at the congress was the legally very restricted research conditions in Germany in the field of human embryonal stem cell research. The participants, including the Spanish Minister for Health, Prof. Dr. Bernat Soria, were united in their opinion that a Europe-wide standardization with regard to such regulations is desirable. This would mean, in particular, a revision of the regulation in Germany and a more precise definition of the legal implications for research in the field.

Shortly prior to the World Congress on October 17, 2007, the four German centers for regenerative medicine, the Translational Centre for Regenerative Medicine (TRM) Leipzig, the Berlin-Brandenburg Center for Regenerative Therapies (BCRT), the Center for Regenerative Therapies Dresden (CRTD) and the most recently awarded Cluster of Excellence "rebirth" (Hanover), met in Leipzig along with other renowned German research groups. Those present agreed to found a national initiative for regenerative medicine in order to more effectively promote the field to the public and to act more commonly in the European research frameworks.

Meanwhile, Fraunhofer IZI has grown to nearly 100 individuals and is pushing the capacity of the rented and, through cooperations, shared spaces. With this in mind, we are anticipating with pleasure the completion of the institute's new main building on the corner of Perlickstraße/Zwickauer

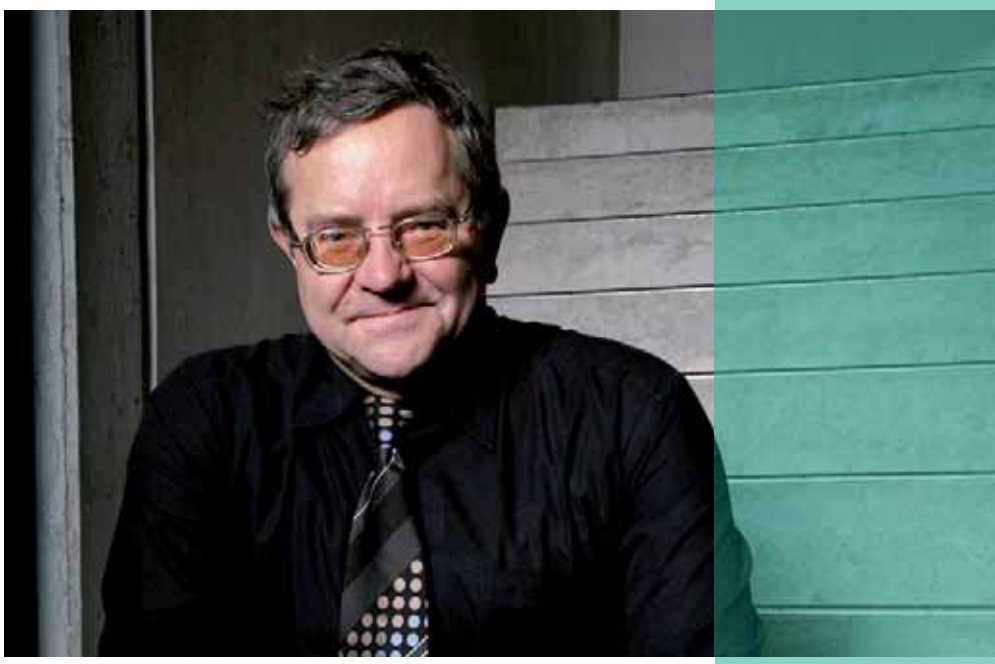
Preface

Straße. The construction progress is running on time and within budget, so that in spring 2008, we will be able to move in. We all expect this to provide a substantial push in motivation and innovation for our work. The unexpected delay of our technically most important laboratory areas, that should be realized in an extended concept, will hopefully be solved in the new year.

Before I commend you to reading the content of our 2007 Annual Report, I must thank all of the staff and colleagues for their fantastic work in 2007. New challenges await us in 2008 that we will enthusiastically meet. Besides the report in your hands, we anticipate publishing, for the first time, in 2008 a service catalog for Fraunhofer IZI. We hope this catalog will help us to better discern and meet the needs and wishes of our partners and customers.

Leipzig, the 1st of February 2008

Prof. Dr. Frank Emmrich
Director, Fraunhofer Institute for Cell Therapy and Immunology



Profile

Cell Therapy and Immunology

In its narrow sense, cell therapy means the transfer of cells to replace lost functions and even to adopt additional active tasks. It also covers the treatment of cells through the repairing of deficiencies. Stem cells can be transferred in order to trigger tissue formation and repair. Cell therapy is hence related to immunology, which deals with cellular defense and monitoring mechanisms. Cell therapy techniques for the targeted strengthening, suppression and regeneration of the immune system, for example in order to stimulate the defense of degenerated cells or to suppress the undesired rejection of transplanted tissue, are expected to be available soon. In addition, a prominent role is played by the development of immunomodulation techniques such as vaccination.

In line with its four core competencies, Fraunhofer IZI is currently divided into 14 thematically clustered groups. Fraunhofer IZI serves clients from the biotechnology industry, suppliers of medical equipment and pharmaceutical companies by performing intelligent, research-intensive services and carrying out development projects. The range of services offered by the institute includes market analyses, technical feasibility studies, and prototype development using human and animal cells and tissues, as well as the conclusive formulation of production and process technologies.

The new building of the institute during construction in April 2007 (above) and the BIO CITY (below).

Biotechniques – Models

In this area, Fraunhofer IZI develops technologies for the cultivation of tissues and cells outside the body (tissue engineering) in order to reconstruct tissues. This includes the development of custom bioreactors and the selection of specific material and surface properties. Fraunhofer IZI also has special expertise in developing techniques for the production of cell and tissue cultures as well as monoclonal antibodies. The institute's in-house production facilities are designed for the manufacture of clinical trial samples. Regarding the production of antibodies, Fraunhofer IZI is also skilled in the downstream processing of raw products. Cell and tissue models developed by our researchers can be used for testing, screening and the immunotoxicological examination of new drugs, cosmetics, food additives and industrial chemicals. The institute offers various small- and large-animal models for therapy development along the course of the pharmaceutical development value chain.

Immunology – Immunomodulation

This area includes the development of methods for the stimulation or suppression of the immune system. One key topic is improving the smooth acceptance of transplants by inducing specific tolerance. Fraunhofer IZI develops techniques to monitor immunoreactivity and to monitor unwanted responses such as GvHD (Graft versus Host Disease). It also develops vaccines on an innovative technology platform using plasmid DNA which are particularly safe, robust and inexpensive.

Cell Therapy – Active Agents

In this area, cells are developed, cultivated and bred for therapeutic purposes. Fraunhofer IZI offers isolation and purification methods for cells from blood and tissue. It also develops special treatment techniques using T-cell clones and natural killer cells as well as vaccination strategies using dendritic cells for tumor treatment. One key area is cell therapy techniques for ischemic diseases such as stroke and myocardial infarction. Projects also include research into methods of preventing the degeneration and aging of cells. Furthermore, the institute explores "dormant" stem cell potential and derives new strategies for drugs able to control tissue growth and regeneration.

Molecular Biology – Individualized Medicine

In the field of molecular biology, Fraunhofer IZI is working on a new technology platform which enables RNA molecules to be identified and ascertained for their potential to effect the intracellular control of signal processes. This provides indications for the development of new drugs. Furthermore, Fraunhofer IZI develops pharmacogenomic and protein-chemistry techniques for the identification of individual-specific differences from which particular disease susceptibility, sensitivity to certain methods of therapy and even the course of disease can be predicted.

History

The institute was officially founded in April 2005. Its first experimental work was conducted under a cooperation agreement with the University of Leipzig at the Max Bürger Research Center, before being continued and extended at Fraunhofer IZI's own laboratory at BIO CITY Leipzig in autumn 2005. This was only possible because 1,500 square meters of laboratory and office space at BIO CITY had been swiftly equipped thanks to smooth cooperation on the part of all those involved. In this context, it should be underlined that a newly devised clean room facility for GMP work in cell and tissue technology was planned, designed, built and validated within the space of just ten months, entering into operation when the first projects were performed there in summer 2006. The city of Leipzig has shown a high level of interest by providing the estate contiguity to the BIO CITY near the city centre. On September 22, 2006, the cornerstone for the institute was laid right next door to BIO CITY for a 4,000 square meter building, which when completed will contain exceptional working conditions. Hardly eight months later, in May 2007, the topping-out ceremony could be celebrated. The occupation of the new premises is planned in March 2008.

Chronicle

April 29, 2005	Institute is founded
October 2005	First laboratories at BIO CITY (rehire)
June 2006	GMP facility opened
July 12, 2006	Institute´s first strategy meeting
September 22, 2006	Foundation stone laid for the first wing of the new institute building
October 22-24, 2006	First Fraunhofer Life Science Symposium
May 8, 2007	Visit by EU-Commissioner responsible for Science and Research and the Saxon minister president
May 31, 2007	Topping-out ceremony for the first wing of the new institute building
October 18-20, 2007	Organizing of the 3rd World Congress on Regenerative Medicine by Fraunhofer IZI
October 18, 2007	2nd Fraunhofer Life Science Symposium

Foundation ceremony of Fraunhofer IZI in the BIO CITY in 2005 (top left), Foundation Stone Ceremony (top right), and the Topping Off Ceremony for the new building (bottom left). The 3rd World Congress on Regenerative Medicine (bottom right).

Management

The structure and operation of Fraunhofer IZI are based on the successful experience of other Fraunhofer Institutes gathered over the years. The director of our institute is Prof. Dr. Frank Emmrich, who is also a professor at the University of Leipzig, where he has headed the Institute of Clinical Immunology and Transfusion Medicine since 1994. This dual position enables the efficient sharing of experience, not to mention the optimal supervision of undergraduate and doctoral dissertations, and provides an excellent basis for cooperation. Both a doctor and an immunologist, Prof. Emmrich spent 13 years as both a researcher and department head at Max Planck Institutes in Freiburg and Erlangen. Over seven of these years he was a professor at the Friedrich Alexander University in Erlangen-Nuremberg.

Administration

The head of the institute is assisted by Patric Nitz – an administrator with an academic background in both management and the organization of staff trainings. He also holds an MBA from a British university and has several years experience managing departments and divisions in large organizational units in the public and private sectors.

Structure

In its current phase of development, Fraunhofer IZI is divided into 14 groups managed by their group leaders as business units. Their budgets are negotiated with the management of the institute every year – and the development and funding of each group largely depend on their success in attracting projects and contracts. Individual groups develop particular competencies which are made available as services not just externally, but also internally. The varied research competencies and services lead to synergies inside the institute and offer new perspectives to customers and research partners.

Facilities

On the premises and in laboratory space currently used, Fraunhofer IZI maintains standard laboratory facilities for biochemistry, molecular biology and cell biology, including a large inventory of equipment which is augmented by systems and instruments that are used cooperatively. For more details, please see the descriptions of the individual groups.

Animal Experiments

The first extension wing of the institute will include a department devoted to animal experiments. Experiments on animals are currently carried out in cooperation with the Faculty of Veterinary Medicine, the Faculty of Medicine and the Max Planck Institute for Evolutionary Anthropology. In addition, projects involving animal experiments have begun with the Faculty of Biology, Pharmacy and Psychology.

GMP Facility

One outstanding achievement in terms of precision and speed is the planning and completion of Fraunhofer IZI's multipurpose GMP facility at the BIO CITY. It was planned, built and approved within the space of just ten months, enabling the first major contract to be started in summer 2006. It was also ensured that the new building would be connected via a bridge so that the GMP facility can continue to be used – hence granting planning certainty to all the partners involved.

In this context, Fraunhofer IZI would like to thank the European Union, the Federal Ministry of Education and Research, the Free State of Saxony, the city of Leipzig and the "Leipziger Stiftung für Innovation und Technologietransfer" for their financial support through the current development phase of the facility.

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.

Dr. jur. Dr. h.c. oec. publ. Albrecht Schmidt (Chair)
Bayerische Hypo- und Vereinsbank AG,
Chairman of the Supervisory Board

Dr. Annerose Beck
Saxon State Ministry of Science and the Arts (SMWK),
Deputy Head of National-Regional Research Centres Administration

Dr. Gabriele Hausdorf
Federal Ministry of Education and Research (BMBF),
Head of the Section of Health Research within the Department of Life Sciences

Dr. Michael Herschel
GlaxoSmithKline GmbH & Co. KG,
Head of Clinical Research

Dr. Eberhard Lampeter
VITA 34 AG,
Chairman

Prof. Dr. med. Gustav Steinhoff
University of Rostock,
Director of the Department of Cardiac Surgery

Prof. Dr. Hans Wolf
University of Regensburg,
Director of the Institute for Medical Microbiology and Hygiene

Financed by the European Union

Federal Ministry of Education and Research

Freistaat Sachsen

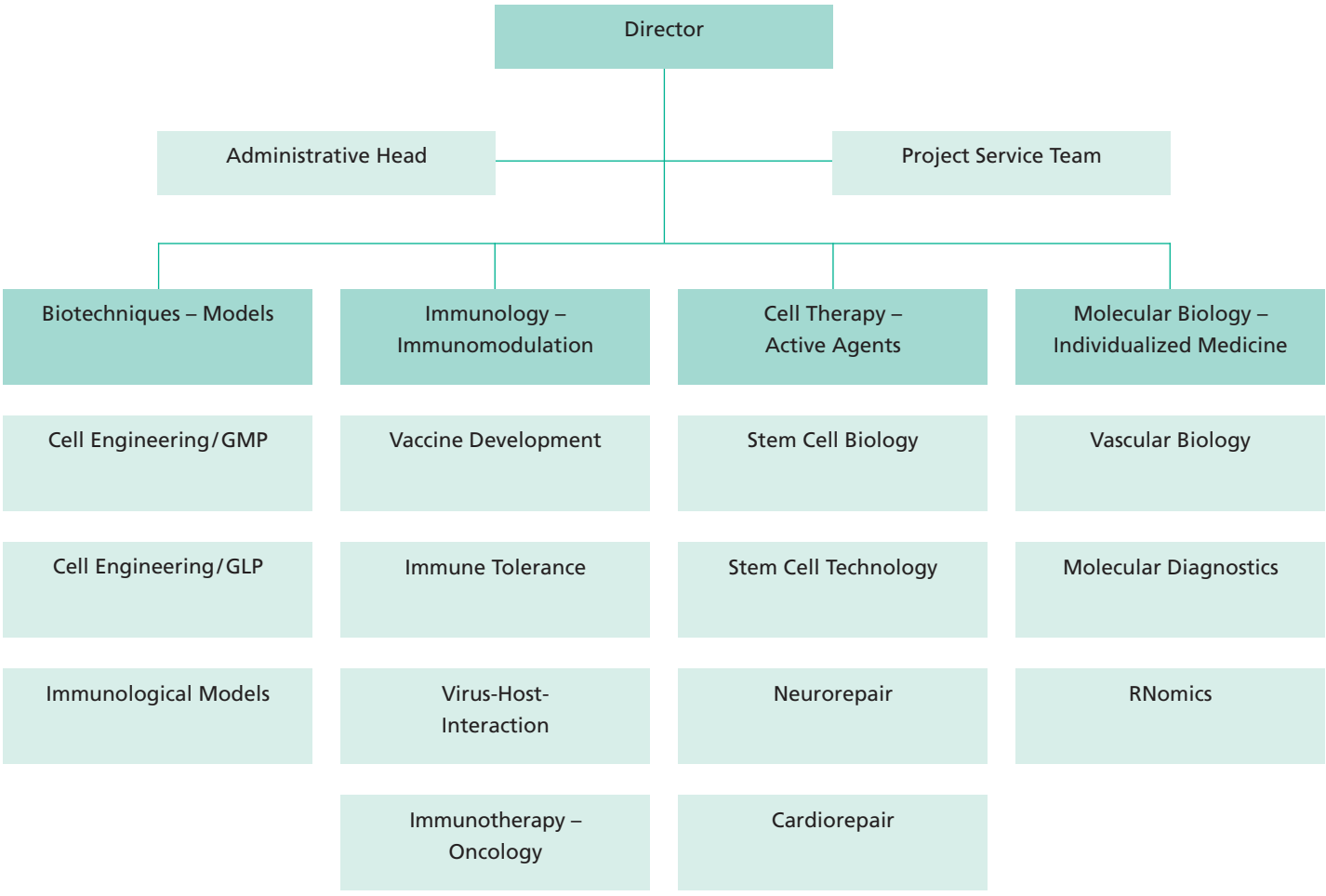
LEIPZIG

Leipziger Stiftung für Innovation und Technologietransfer

Director of Fraunhofer IZI
Prof. Dr. Frank Emmrich
Medicine, Immunology
Phone: +49 (0) 341/355 36-9105
frank.emmrich@izi.fraunhofer.de

Administrative Head
Patric Nitz
Law, Administration
Phone: +49 (0) 341/355 36-9200
patric.nitz@izi.fraunhofer.de

Project Service Team
Dr. Wilhelm Gerdes
Biology, Business Development
Phone: +49 (0) 341/355 36-9300
wilhelm.gerdes@izi.fraunhofer.de



Biotechniques – Models

Cell Engineering/GMP
Dr. Gerno Schmiedeknecht
Biochemistry, Biotechnology
Phone: +49 (0) 341/355 36-9705
gerno.schmiedeknecht@izi.fraunhofer.de

Cell Engineering/GLP
Dr. Jörg Lehmann
Biology, Immunology
Phone: +49 (0) 341/355 36-1205
joerg.lehmann@izi.fraunhofer.de

Immunological Models
Dr. Manja Kamprad
Biology, Immunology
Phone: +49 (0) 341/97 25-830
manja.kamprad@izi.fraunhofer.de

Immunology – Immunomodulation

Vaccine Development
Dr. Sebastian Ulbert (Laboratory)
Dr. Matthias Giese (Head of Group)
Infection Biology
Phone: +49 (0) 341/355 36-2106
sebastian.ulbert@izi.fraunhofer.de

Immune Tolerance
Dr. Stephan Fricke
Medicine, Immunology
Phone: +49 (0) 341/355 36-2205
stephan.fricke@izi.fraunhofer.de

Virus-Host-Interaction
Dr. Jörg Baumann
Infection Biology, Virology
Phone: +49 (0) 341/355 36-2505
joerg.baumann@izi.fraunhofer.de

Dr. Sabine Breun
Infection Biology
Phone: +49 (0) 341/355 36-2506
sabine.breun@izi.fraunhofer.de

Immunotherapy – Oncology
Dr. Christoph Schimmelpfennig
Hematology, Oncology
Phone: +49 (0) 341/355 36-3105
christoph.schimmelpfennig@izi.fraunhofer.de

Cell Therapy – Active Agents

Stem Cell Biology
Dr. Alexandra Stolzing
Stem Cell Biology
Phone: +49 (0) 341/355 36-3405
alexandra.stolzing@izi.fraunhofer.de

Stem Cell Technology
Dr. Nicole zur Nieden
Stem Cell Biology
Phone: +49 (0) 341/355 36-3305
nicole.zurnieden@izi.fraunhofer.de

Neurorepair
Johannes Boltze
Medicine, Neurology
Phone: +49 (0) 341/97 25-820
johannes.boltze@izi.fraunhofer.de

Cardiorepair
Dr. Alexander Deten
Medicine, Cardiophysiology
Phone: +49 (0) 341/355 36-3505
alexander.deten@izi.fraunhofer.de

Molecular Biology – Individualized Medicine

Vascular Biology
Dr. Andreas Schubert
Biology, Molecular Biology
Phone: +49 (0) 341/355 36-5105
andreas.schubert@izi.fraunhofer.de

Molecular Diagnostics
Prof. Dr. Ulrich Sack
Medicine, Immunology
Phone: +49 (0) 341/97 25-506
ulrich.sack@izi.fraunhofer.de

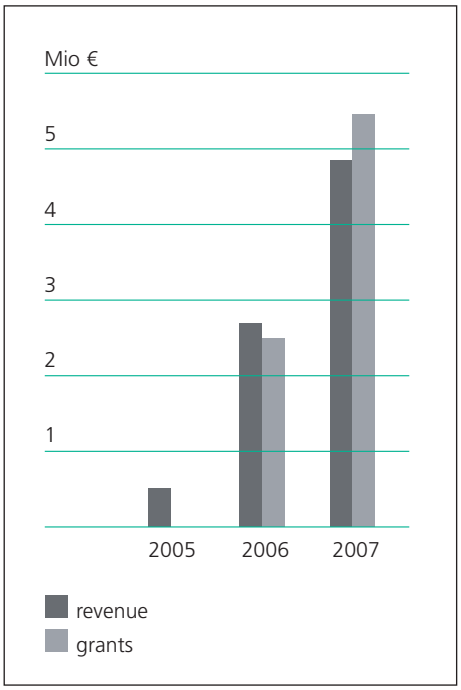
RNomics
Dr. Jörg Hackermüller
Bioinformatics
Phone: +49 (0) 341/355 36-5205
joerg.hackermueller@izi.fraunhofer.de

Dr. Antje Kretzschmar
Biochemistry
Phone: +49 (0) 341/355 36-5206
antje.kretzschmar@izi.fraunhofer.de

Fraunhofer IZI in Figures

Budget

In 2007, the budget was consolidated to 4,890,000 euros through a reduction of accrued costs in the amount of 646,000 euros. For the first time, 114,000 euros of EU revenues were achieved and an overproportional increase in industry revenues totaled at 605,000 euros.



Budget

Projects

The research activities at Fraunhofer IZI continue to be affected by active acquisitions from domestic and foreign sources. The special challenge in 2007 was again in the acquisition of industry revenues which nearly tripled, with an increase from 240,000 euros in 2006 to 605,000 euros in 2007; they account for 12.4 percent of the actual costs (4,890,000 euros). We are pleased that a large project with the federal institute for agriculture and nutrition was completed in 2007, which we anticipate will function as a reference for future projects. With cooperations like this one, the Fraunhofer IZI is building a new competency in the areas of vaccines for domesticated animals and in zoonosis projects.

Contact
Patric Nitz
Phone: +49 (0) 341/355 36-9200
patric.nitz@izi.fraunhofer.de

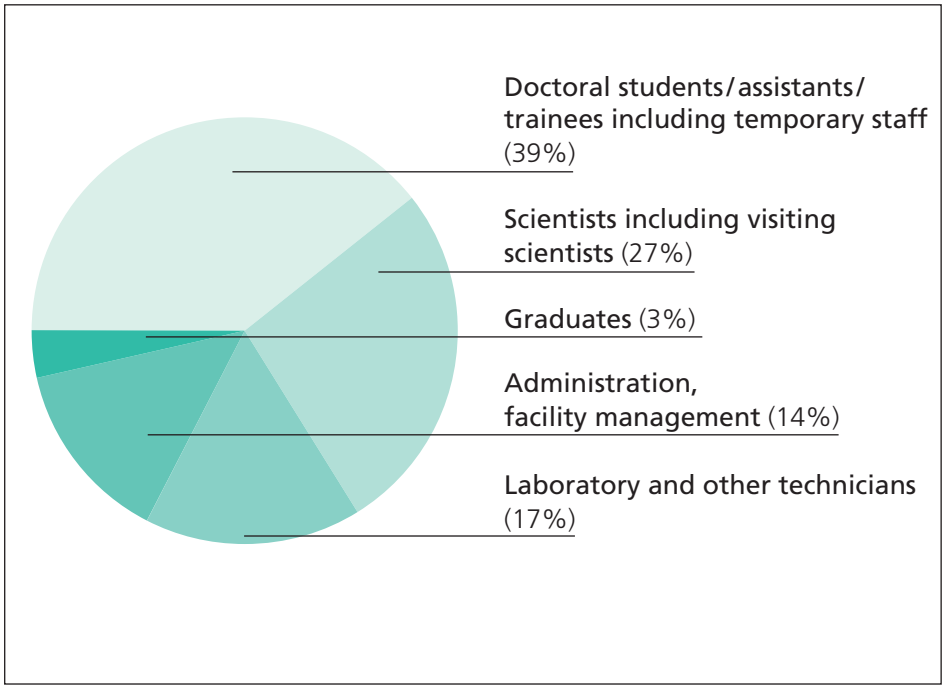
The term "organization" has the greek root "organo" which means "support, tool." This should serve to remind us what an organization really should be: It should not take center stage, but be a tool or support, in order to make work easier, solve problems more quickly and complete tasks more efficiently.

Overview of the Projects

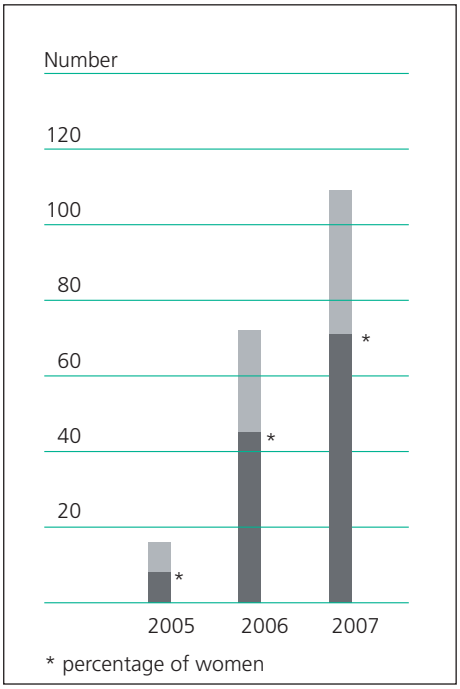
	Number 2006	Volume 2006	Number 2007	Volume 2007	Increase
German national and regional government	2	1,574,000 €	8	3,032,000 €	193%
EU	1	15,000 €	2	114,000 €	760%
Industry Projects	7	240,000 €	18	605,000 €	252%
Other	5	870,000 €	18	1,139,000 €	131%
Total	**15**	**2,699,000 €**	**46**	**4,890,000 €**	**181%**

Human Resources

In 2007, many new staff joined the Fraunhofer IZI. From the beginning to the end of the year, the number of staff increased by 38 to 109. Twenty-nine of the new staff are employed as research associates, 15 are in the administration. The remainder are 18 technicians for the laboratories and other areas, as well as 4 postgraduates. The number of employees in part-time positions (graduate assistants, interns) or as doctoral candidates increased to 43. Particularly of note is the high percentage of female staff: 71 members of staff are female (65 percent). Thereby, Fraunhofer IZI joins the few institutes in the Fraunhofer-Gesellschaft that have significantly more women than men employed; we hope to continue this trend in the future. Also notable is that in 2007 two of our female staff entered maternity leave. The administration has further professionalized itself through the employment of its own IT-specialist and an operations engineer; this extends our preparedness for the opening of the new building in 2008.



Workforce composition 2007



Employees

Customer Service

Our Partners

MagnaMedics GmbH

Research Contracts

The institutes of the Fraunhofer-Gesellschaft view themselves as professional research service providers. They render their service on the basis of contracts that ensure content and deadline conditions of the clients and that also reflect client's own needs and specifications. Of course, in the first phase, clients may ensure themselves confidentiality and non-disclosure of the contracted project.

Fraunhofer IZI has standardized contracts for phase 1, but is also prepared to make use of partner or client contracts that have been legally reviewed by the Fraunhofer-Gesellschaft. The contacts for this phase and in following phases of partnership are the members of the Project Service Team (PST) and/ or the group leaders in whose field the agreed research services will occur.

In phase 2, the cornerstones of a contract are defined in a term sheet by the partner institutions. To effectively plan the targets, the contract timeframe and financial development are also sketched at this phase. The views of both parties about IP rights and utilization options will be agreed in essential points.

On this basis, the staff of Fraunhofer IZI prepares an offer or draft contract that will be discussed and negotiated in phase 4.

After review by the legal advisors of the partners, the agreement of the contract and its signing follows in phase 5.

Phase 1 – Confidentiality Agreement
Signing of a non-disclosure agreement. Original text may be from the partner or Fraunhofer-Gesellschaft.

Phase 2 – Term Sheet
Definition of the cornerstones between the partners (IP rights, utilization rights, contract timeframe, project plan, financial development).

Phase 3 – Offer
Drafting of the contract based on the project plan and cornerstones as defined in phase 2.

Phase 4 – Contract negotiation
Discussion and finalization of the contract by the partners.

Phase 5 – Contract agreement
Signing of the research contract after review and, if necessary, changes by the legal advisors of the partners.

Project Work

The key contact for clients is either the group leader or a member of the business development team (PST). Both can supply the potential client with the necessary information. Assuming mutual interest in cooperation, Fraunhofer IZI has a non-disclosure agreement or a memorandum of understanding drawn up.

Project applications are painstakingly compiled for submission to public funding bodies and industry using the internal technology platforms at Fraunhofer IZI and the group's or groups' scientific competencies. In doing so, the team scrutinizes both the opportunities and the risks of projects and underpins applications by means of patent, literature and market research.

Afterwards, the partners compile a joint action plan, resulting in a project outline or application. This application provides the basis for subsequent contract negotiations conducted jointly between the partner, Fraunhofer IZI and the Fraunhofer-Gesellschaft. While the project is being carried out, the partner is kept abreast of its progress by the group leader or a team member at agreed regular intervals. Any scientific queries are addressed to the group leader. Following the completion of the project, a report will be written which is then submitted to the partner.

Project Service Team

Services

- project acquisition
- project planning, coordination, management and marketing
- fundraising support
- public relations
- business development
- organizing and realization of scientific events
- planning and implementation of career development events

More services of the group can be found on page 31.

The PST or business development team at Fraunhofer IZI is of crucial importance to the initiation of projects. Team members support the individual groups every step of the way from evaluation to final reporting. In addition to many years of experience in scientific work, this includes a particular understanding of the way public authorities and commercial companies operate.

The primary function of this department is identifying and contacting potential cooperation partners. Contact is sometimes made through attending trade shows, conferences and conventions. Alternatively, new contacts are developed through existing partnerships that are continuously nurtured. In addition to national partnerships, the business development team is increasingly striving to set up international cooperation. Apart from pinpointing potential

Contact
Dr. Wilhelm Gerdes
Phone: +49 (0) 341/355 36-9300
wilhelm.gerdes@izi.fraunhofer.de

The identification and initial contact of potential cooperation partners and the evaluation of resulting projects are main charges of the PST.

Project Service Team (left to right): Christina Kühn, Dr. Wilhelm Gerdes, Dr. Sonya Faber, Susann Bachmann, Dr. Christian Zilch, Jens Augustin, Michaela Grahn.

cooperation partners, the team also busies itself intensively with applying for funding for the mutual interest of its scientists and partners. It sifts through funding calls from the national and regional governments in Germany as well as throughout the European Union and forwards suitable ones to the relevant groups at Fraunhofer IZI. Furthermore, the members of the business development team support the individual groups in drawing up project outlines and applications. The team forms the central interface of the institute and maintains close contact with grant officers at financing institutions in order to enable not just optimal communication, but also the successful controlling of project documentation.

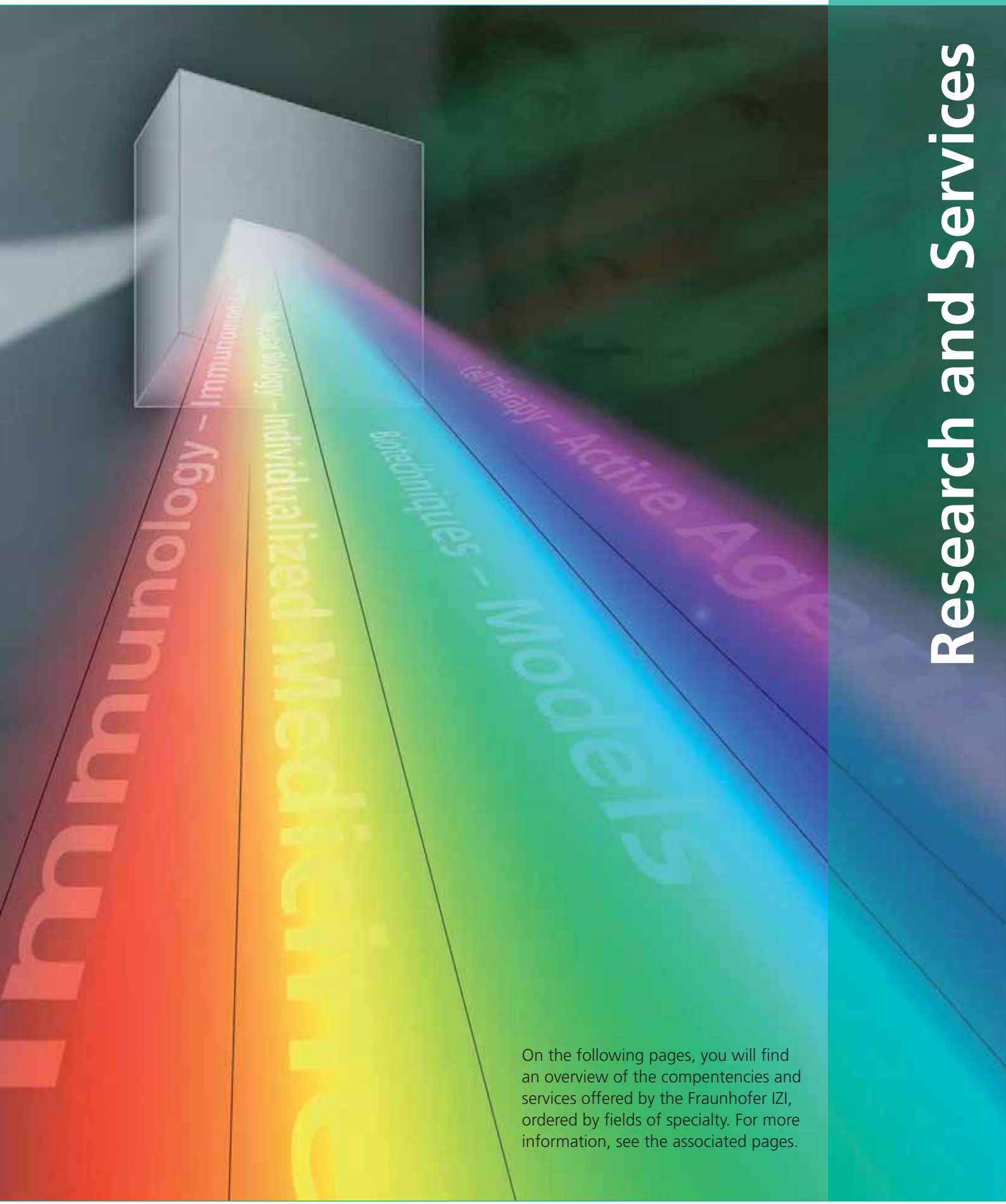
Representing the institute and public relations is a further focus for the PST. The PST takes on the responsibility of representing the institute at the majority of public events and conventions, thereby relieving the research staff from this time commitment. Furthermore, the team organizes internal career development and informative events. By organizing scientific symposia and congresses, the PST makes another important contribution to the national and international image of the institute. In 2006, we founded the Fraunhofer Life Science Symposium. This event was successfully repeated in 2007 and is planned to occur annually. This event series contributes with its changing main themes to the continual extension of the Fraunhofer IZI's scientific and contact spectra. With this in mind, we ventured, with the 2007 symposium, to explore regenerative medicine in the field of veterinary medicine. The topic was surprisingly well received and demonstrated clearly how worthwhile it is to probe new topics under the banner of application-oriented research; thus are we able to lay the foundations for new research communities.

Cooperation partners are often scientific research institutions and universities, but they are primarily businesses from pharmaceutical or biotechnology industry, medical technology, health economy or even the food industry. Conventions, symposia, congresses or direct contact are our main avenues of networking.

Fraunhofer Lines

Self-made prisms enabled Joseph von Fraunhofer to discover dark lines in the spectrum of sun light in 1814. Fraunhofer, himself, determined the exact wavelength of 570 lines. Chemists discovered later that every chemical element is associated to a specific spectral line. The lines are formed by gasses in the photosphere that absorb a part of the sun light.

Research and Services



On the following pages, you will find an overview of the compentencies and services offered by the Fraunhofer IZI, ordered by fields of specialty. For more information, see the associated pages.

Small Animal Models (Mouse/Rat)

infection immunology *(salmonella enterica, borrelia burgdorferi)*	development of preclinical therapy models	40, 56
	development and analysis of antibacterial active agents	72
chronic arthritis (collagen induced arthritis model, human/murine SCID-arthritis)	development of active agents and testing antirheumatic agents with different profiling	40, 80
chronic inflammatory bowel disease (TNBS-colitis)	development and testing of active agents	40
xenogenic and allogeneic GvHD (transgenic mice)	development of cell based therapies and active agents for treatment of GvHD	48
skin grafting	skin transplantation	48
cell transplantation procedure in rodents	intravenous, intra-myocardial and intra-peritoneal application of cell grafts	48, 56, 64, 70
ischemic heart dieseases (myocard infarction, ischemia reperfusion)	testing of therapies and active agents	70
functional analyses in ischemic heart diseases	induction of hibernation and ischemic preconditioning *(in vivo)*	70
	heart hypertrophy/chronic cardiac remodelling (aortic constriction or pharmacologically by norepinephrine)	70
	measurements of right and left heart function with ultraminiatur tip-catheters and by echocardiography	70
	MI-size measurements (IA/AAR)	70
focal cerebral ischemia (stroke)	testing of active agents, neuroregeneration, neuroprotection	66
therapy models for bone regeneration	therapy development, compound screening	60

Large Animal Models (Sheep/Dog)

model for preclinical evaluation of new blood products (dog)	preclinical evaluation of new blood products and cell products	40
therapy model focal cerebral ischemia (stroke; sheep)	testing of active agents, neuroregeneration, neuroprotection *in vivo*	66

Cell Culture Models

HIV and other pathogens	test system for mucosal virus transmission for *in vitro* and *in vivo* studies	52
	development of antiviral strategies	52
differentiation of hematopoietic cells	development of cell lines and expression systems for *in vitro* and *in vivo* studies	52, 56, 64
modulation of immune cells	modulation and targeted alteration of primary cells	52, 56
GvHD	development of antibody based therapies, learing of patho mechanisms	48
	testing of monoclonal antibodies	40, 48
	development of cell-based therapies for transplantations	48
neuronal hypoxia and ischemia in differentiated and undifferentiated cells	development of cell based therapies for the treatment of stroke	66
monitoring models	monitoring of experimental therapies, process development and process optimization for stroke	66
embryonic stem cell assays, embryotoxicity assays	process development of bioreactor, expansion and differentiation of cells	60
culturing myocardial cells	testing of active agents	70
screening models	*in vitro* and *in vivo* quality controls for stem cell processes	44, 56, 60
	screening for active agents and testing, especially antidestructive and antiinflammatory drugs	80
bioreactor/suspension culture	identification of 3-dimensional stem cell niches	60
	training of cells for transplantation into mechanically active sites	60

Active Agents

development and testing of active agents	for therapy of myocardial infarction	70
	for therapy of stroke and neuroprotection	66
	for therapy of cartilage and bone defects	60
	for antiviral therapies	52, 56
	for adult stem cells (HSC, MSC) (in vivo stem cell tests, cell stimulation, cell modulation)	44, 56, 64
	for embryonal and early stem cells (ESC, MLPC)	56, 60
	for antiviral vaccines and active compounds	52
	for biomarkers (aging, stress and oxidative damage in cells)	64
	for cariogenic bacteria (also screening and therapy development)	72
	for chronic arthritis and chronic inflammatory bowel diseases	40, 80
	immunmodulating and antiinflammatory active agents	56, 80
	pharmacological testing (e. g. antibiotics and immunosuppressiva)	40
production of antibodies (monoclonal and polyclonal)	development, production, purification, conjugation	40

Cell Technologies

isolation of cells	process development cell preparation from body fluids and tissues	40, 44, 56, 64, 66, 80
cell separation, cell preparation, cell analysis	cell function assay (e. g. Lymphocyte transformation test, CFU, microbicidy, phagocytosis, colony tests, monocytes, granulocytes)	40, 44, 56, 64, 66, 80
	phenotyping, functional characterization	40, 44, 56, 66, 80
	separation of highly purified cell preparations	40, 56, 80
	karyotyping, identification and characterization of cell preparations	80
laser assisted microdissection	single cell analysis in tissue	80
cell- and tissue analysis	stem cell based therapy development	56, 64, 66, 72
flow cytometry (analytic and preparative)	cell analysis, cell sorting, cell characterization, immunocytometric diagnostics	40, 44, 52, 56, 60, 64, 80
fluorescence activated cell sorting (FACS)	detection and characterization of surface molecules on cells before and after transplantation procedure	44, 48, 56, 60
purification of specialized immune cells	production of accurately defined grafts	44, 48, 56
cell culture technologies	development of tumor specific and cytotoxic cell lines (T-cell based, dendritic cells, NK-cells, NK-T-cells)	56
	cytokin induced killer cell expansion technology (human and murine)	56
tumor cell bank (murine and human) with different cell lines	development and tests of different animal models	56
bioreactor technologies for the expansion/ differentiation of stem cells	quality control for stem cell processes	56, 60
	differentiation of stem cells under biomechanical stimulation	72
fluorescent reporter embryonic stem cell lines	optimization of media for expansion/directed differentiation of stem cells and characterization of signal transduction pathways	52, 56, 60
in vitro stem cell assays (e. g. osteogenesis)	quantification of soluble mediators in body fluids	44, 60
in vivo stem cell assays for HSC and MHC	analysis of biocompatibility of drugs and scaffolds	44, 56
	diagnostic immunoassay	44, 56
	analysis of cytokines in tissue and fluids	44, 56
development of *in vitro* assays, process development	development of immuno assays for research and diagnostics, antigen generation (recombinant, native)	40, 56
assays for differentiation, methylation, pluripotency	evaluation and quality control in stem cells and reprogramming	56, 64, 60
adult stem cells (mesenchymal & hematopoietic)	development of cell based therapies (Alzheimer´s disease, diabetes)	56, 64
fusion, partial cloning, reprogramming	reprogramming of somatic body cells to a progenitor stage	64
vitrification and cryopreservation	improving storage of cells and cell products	64
biomarkers for aging, stress and oxidative damage in cells	characterization of aged cells and tissue	64, 72
immune modulation	transduction of stem cells including expression analysis	52
cytometric bead array (CBA)	detection of soluble molecules interaction on immune cells (human and murine)	44, 48, 56

Immuno Technologies

immunotoxicology, neurotoxicology	immunotoxicity and neurotoxicity studies and screenings (also under GLP)	40, 44, 80
immunohistology/histology	production and analisis of histology slides (animal models)	48, 56, 66, 70
	immunohistological analysis and quality insurance	80
immunopathology	immunopathological analysis and quality insurance	80
immunocytochemistry	immunocytochemical detection of cells and proteins	40, 56
ELISA-technologies	quantitative cytokine and antibody analytics in fluid samples	40
diagnostic and analytic immunoassays	development, optimization and execution of immunoassays	80
purification of monoclonal antibodies from hybridoma	allocation of monoclonal antibodies for experimental/therapeutic questions	40

Proteomics

high throughput analytics (proteomics)	expression- and proteomics analysis (2D GE, DIGE, also under GLP)	40
protein purification	protein purification by preparative HPLC (e. g. antibodies, cytokines, rekombinant, native)	40
protein analytics (SDS-PAGE, IEF, Western Blot)	qualitative and quantitative analysis of proteins	40, 52
biomechanical stimulation of cells under different flow profiles with and without medication	allocation of RNA and proteins after flow application	72
quantification of peptides	detection and profiling of peptides in body fluids	80
automatized mass spectrometry for DNA and peptides (high throughput)	individual response to different drugs (pharmacogenomics)	80

Molecular Biological Technologies

production of standardized virus charges	transduction of different cell types	52
	investigation of antiviral components	52
development of new vectors based on retroviruses, other viruses and nonviral	production of customized expression systems	46, 52
molecular biological analysis of retroviral replication	investigation of antiviral components, quantification based on real-time PCR	52
mutation analysis	molecular biological investigation of protein function	52
SNP analysis in human genome	services with cooperation partners	66
intracellular interaction (with state-of-the-art methods)	pathogen-cell, protein-protein, protein-cell interactions	52
immune modulation	transduction of different cells (stem cells, primary cells, cell lines) including expression analysis	52
quantitative PCR	production of plasmids, quantification after cell transplantation	48
transfection of artificial chromosomes in primary cells	expression studies in different cells	72
analysis of mRNA and protein expression of relevant genes/proteins	testing of biocompatibility of plastic surfaces	72
microRNA and ncRNA transcriptomics	miRNA and ncRNA isolation from cell culture, tissue, or blood	76
	miRNA/ncRNA identification and quantification using microarrays, tiling arrays, quantitative RT-PCR, or ultrahighthroughput sequencing	76
	development of miRNA biomarkers	76
molecular and cell biology of ncRNAs	subcellular distribution of ncRNAs and miRNAs	76
	overexpression and knock down of miRNAs and ncRNAs	76
	physiological effects of aberrant expression of miRNAs and ncRNAs	76
	identification of binding partners (targets) of miRNAs and ncRNAs	76
	development and testing of ncRNAs as agent candidates	76
bioinformatics	analysis of transcriptome datasets	76
	analysis of ultra high throughput sequencing datasets (454, Solexa, RNASolid reads)	76
	annotation and classification of novel transcripts	76
	prediction of RNA structures and interaction partners (targets)	76
microarray technologies	accomplishment of all Affymetrix arrays available (expression, SNP, tiling arrays)	76
	genome wide tiling array experiments for identification of novel transcripts and trasnscript structure	76
	ChIP-on-chip experiments with promotor- and genome wide tiling arrays	76
	development of custom arrays and accomplishment of custom array experiments (combimatrix and nimblegen)	76
	custom tiling arrays – mapping of certain genome regions	76
	custom miRNA arrays comprising known and predicted miRNAs	76
chromatin immunoprecipitation on chip	genome wide measurement of transcription factor binding and epigenetic properties like methylation patterns	76
quantification of oligonucleotides	detection and profiling in fluid samples	80
automatized mass spectrometry for DNA and peptides (high throughput)	individual response to drugs (pharmacogenomics)	80
molecular diagnostic	diagnostic gene profiling for clinical approaches	80
	development and validation of laboratory diagnostic processes	80
molecular analyses in ischemic heart diseases	analysis of gene and protein expression (qRT-PCR, microarry, western-blot)	70
single cell PCR technology	single cell genome analysis	72

Vaccine Development

platform technology DNA vaccines	development of DNA vaccines for human and veterinary medicine	46
zoonosis and parasites research	development of vaccines	46
	development of vector-based vaccines	46
	development of non-viral vectors	46

Imaging

fluorescence microscopy	process development, cell separation, cell application	44, 56, 66, 70
	demonstration of cell surface molecule interaction on immune cells	48, 52
immunohistochemistry	detection of different labeled cells in tissues	56, 66
confocal- and electron microscopy	services with cooperation partners	56, 66
detection of transplanted cells	y-chromosome *in situ* hybridization	60
bioluminescence imaging	imaging of effector cell lines and/or target cells *in vivo*	56

Other Technologies

anesthesia of rodents	realization of different kinds of anesthesia	48, 56
tumor cell bank (murine and human) with different cell lines	development and tests of different animal models and transplantation models development of animal models for cns	56 66
quantitative gene expression analysis by real-time PCR	utilizing established cell culture models	52, 60
radiation of animals and cell biologics	x-ray procedure for different irradiation doses	48
histology/immunohistology	production and analysis of histological slides (animal models)	48, 70
biomarkers for aging, stress and oxidative damage in cells	evaluation of anti-aging effects of substances *in vitro* and in an animal model	64
small and large animal models (in cooperation with the University of Leipzig)	development of drug delivery systems clinical studies	56 56
behavioral phenotyping (cns) development of behavioral test systems (cns)	monitoring of therapies	66 66
osteogenesis and chondrogenesis	biomaterial assessment with cells and tissues (biocompatibility) analysis of pluripotency and lineage specific differentiation markers	60 60
fluidic mechanics (rheology)	expression profiling of endothelial cells and fibroblasts under stress situation	72
chemotherapy in animal models	testing of chemotherapeutical effects on organs and tissues testing of hematotoxicity of chemotherapeutic agents and computational design of chemotherapeutic regimes (in cooperation with the University of Leipzig)	48 44

Large Instrumentation

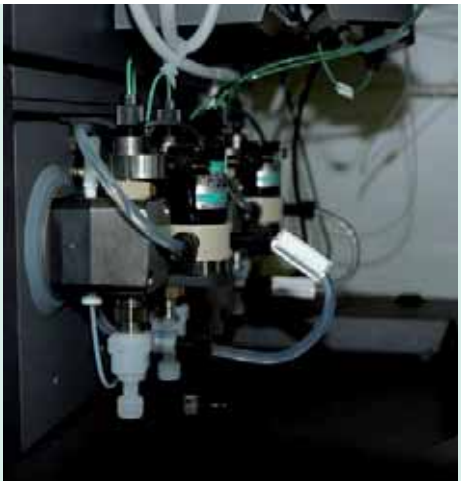
pharmaceutical clean room facility for aseptic manufacturing of investigational medicinal products	provision of clean rooms for manufacturing projects of partners with own pharmceutical responsibility	36
quality control laboratory with qualified analytical devices	performing of GMP-compliant quality controls for autologous and allogeneic cell-based therapeutics and other biologicals	36
laboratory for GLP and quality control – cell biology, immunology and protein biochemistry	GLP studies, quality control	40
imaging facility (fluorescence and bioluminescence imaging)	*in vivo* imaging (migration, survival, cytotoxicity, *in vivo* tumor model)	56
virological work in BL-3 laboratory	testing of antiviral vaccines and active agents against HIV	52
experimental imaging MRT and CT (rat and sheep)	monitoring of therapies (in cooperation with the University of Leipzig)	66
experimental imaging PET (sheep)	monitoring of therapies, development of behavioral tests (in cooperation with the University of Leipzig)	66

GXP-Services

services under regulatory obligations	services under GLP, GMP and DIN/EN/ISO 15189	36, 40
good laboratory practice (GLP)	design of GLP conform process development	40
good manufacturing practice (GMP)	manufacturing of therapeutic antibodies	36
	manufacturing of therapeutic recombinant glycoproteins	36
	manufacturing of autologous and allogeneic cell-based therapeutics	36
	set-up, validation of GMP-compliant manufacturing processes (process development)	36
	storage and cryo-preservation of master and working cell banks	36
	performing of quality controls for cell-based therapeutics and biologicals	36
	consultancy regarding set-up and validation of quality controls according to ICH Q2A/Q2B	36
	consultancy regarding set-up of GMP quality assurance systems	36
	consultancy regarding applications for manufacturing authorizations according to §13 AMG	36
good clinical practice (GCP)	design and supervising of clinical trials in cooperation with nearby partner institutions	24, 56

Other Services

dyslexia studies		66
bioinformatics	analysis of ultra high throughput datasets (sequencing data, transcriptoma data)	76
design and control of antiviral therapeutic concepts	under BL-2 and BL-3 conditions	52
biosafety: activation and mobilization of endogenous retroviruses	testing of cell culture systems and tissues for biosafety	52
consultancy	project funding	24



GLP-Services

"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 Organisation for Economic Co-operation and Development (OECD) that were devised following the EC-Directive, which were incorporated into German law and anchored in the chemical law ("Chemikaliengesetz"). In paragraphs 19a to 19d, the scope and types of controls in Good Laboratory Practice are legally set.

Good Laboratory Practice, like 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.

Services Offered

- contract research from concept to proof-of-principle
- therapeutic substance development
- new diagnostic systems as well as technologies for the application of medicaments
- biosensor and biochip technologies
- preclinical evaluation of therapeutics for humans and animals
- adherence to national, EU and FDA regulations
- all development and evaluation processes are GLP-conform

Customer-specific development of immunologic reagents

- antibodies (poly and monoclonal)
- antigens
- immunoconjugates (enzymes, fluorochrome, biotin)
- reference sera

Development and validation of immunologic assay systems

- ELISA-Techniques (different detection systems)
- immunoblot techniques
- lateral-flow based precipitation assays
- agglutination assays
- immunoprecipitation assays
- flow cytometry assays
- cell-based *in vitro* assays

Development and validation of individual diagnostic assays

- ELISA for antibody detection
- ELISA for antigen detection
- marker-vaccine-specific assays

Development and validation of experimental animal models for pathogenesis, cytotoxicity and therapy studies

- dose-answer studies
- single component studies
- two component studies
- transfection studies

Contact

Dr. Jörg Lehmann
Phone: + 49 (0) 341/355 36-1205
joerg.lehmann@izi.fraunhofer.de

GMP-Services

Fraunhofer IZI operates a 450 sqm GMP-compliant clean room facility.

Through the flexible design, the facility is especially attractive for new biotechnology companies that seek to bring newly developed active ingredients and 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. Most of the available clean room suites are specialized for processes associated with manufacturing of human autologous or allogeneic cell-based therapeutics (e. g. tissue engineering products, stem cell preparations, cancer vaccines). One suite is designed for the manufacturing of therapeutic recombinant proteins and antibodies in small scale (for phase I to early phase II trials).

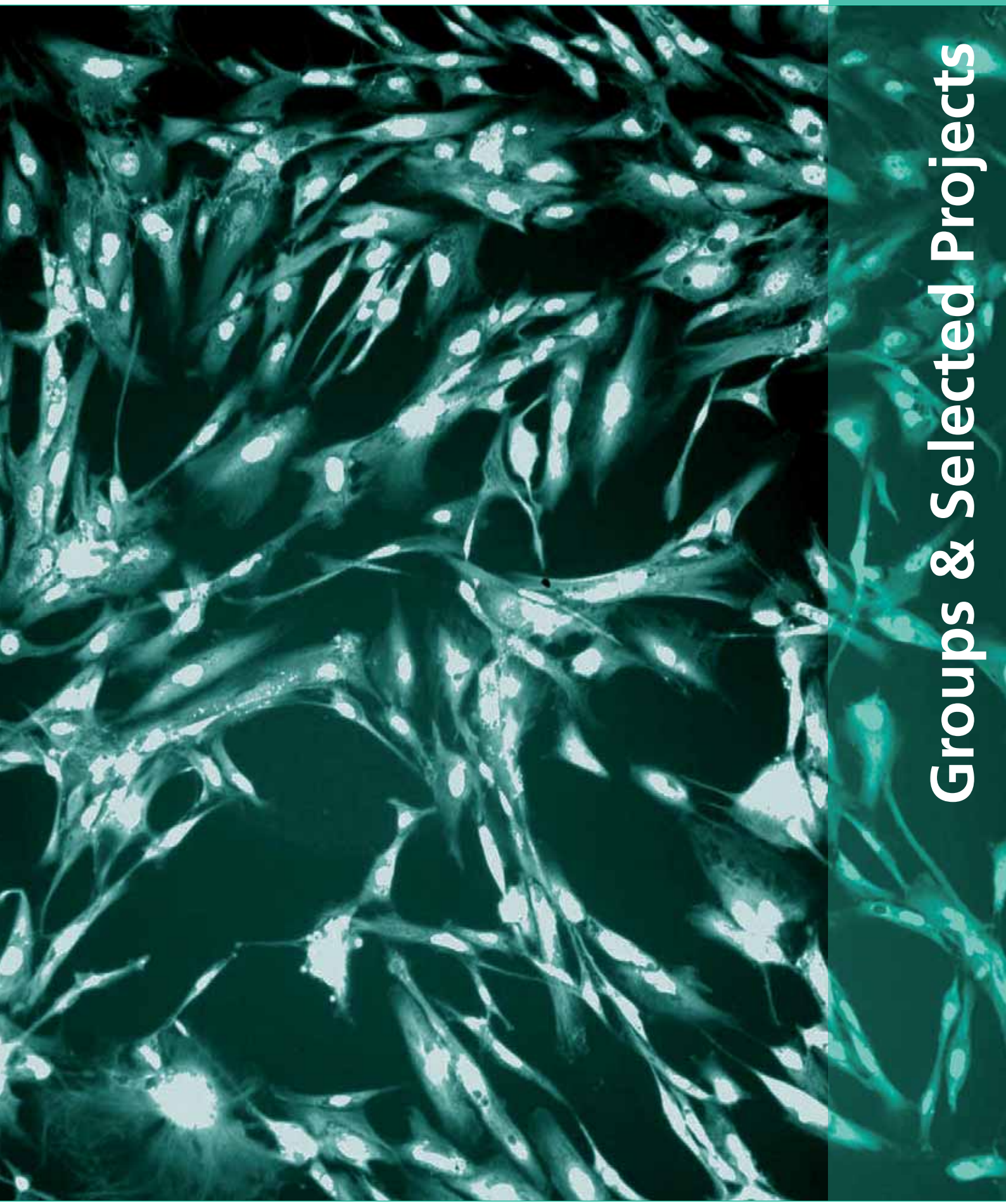
Besides the clean rooms and the technical and, respectively, regulatory infrastructure, the Fraunhofer IZI offers assistance for the set-up and validation of GMP-compliant manufacturing processes as well as for obtaining a manufacturing authorization according to §13 of the AMG.

Services Offered

- GMP-compliant process development
- GMP manufacturing of different cell-based therapeutics (autologous and allogeneic cell-based therapeutics, e. g., tissue replacement/ tissue engineering products, adult stem cell preparations, cancer vaccines, gene therapeutics)
- GMP manufacturing of biologicals based on mammalian cells for phase I or early phase II clinical trials (e. g. therapeutic recombinant glycoproteins and monoclonal antibodies)
- provision of a qualified person according to §14 AMG
- consultancy services in regard to design and validation of GMP-compliant manufacturing processes
- support for obtaining an official manufacturing authorization according to §13 AMG
- provision of separate clean room suites for manufacturing of pharmaceutical products
- transfer of projects from research and development to a GMP-compliant level
- manufacturing, cryo-preservation and storage of master and working cell banks

Contact

Dr. Gerno Schmiedeknecht
Phone: + 49 (0) 341/355 36-9705
gerno.schmiedeknecht@izi.fraunhofer.de



Groups & Selected Projects

Cell Engineering/GMP Group

Products/Services

- provision of clean rooms for manufacturing projects
- manufacture of autologous cell-based therapeutics
- consultancy regarding applications for a manufacturing authorization according to §13 German Drug Act
- storage and cryo-preservation of master and working cell banks
- performing quality controls for cell-based therapeutics

Competencies

- pharmaceutical clean room facility for aseptic manufacturing of investigational medicinal products with references
- quality control laboratory with qualified analytical devices
- comprehensive experience in process development
- highly qualified personnel for manufacturing, quality control and quality management

More services of the group can be found on page 31.

Selected Project: Skin from Hair Roots

Background

Chronic wounds present a challenge for physicians as well as for the affected patients. Despite cause-specific treatments, for example, for diabetes, arterial obstructive disease or chronic venous insufficience, wounds often heal unsatisfactorily. This means, besides enormous costs for the health industry, that affected patients often suffer a lowered quality of life over a long term. Cell therapeutic treatments

Contact

Dr. Gerno Schmiedeknecht
Phone: +49 (0) 341/355 36-9705
gerno.schmiedeknecht@izi.fraunhofer.de

This group maintains modern clean room facilities for manufacturing of investigational medicinal products according to Good Manufacturing Practice (GMP). Our expertise is primarily in the areas of cell-based therapeutics (e. g., tissue engineering products), therapeutic recombinant glycoproteins and antibodies. Our services span all phases from process development to the manufacturing of investigational medicinal products.

Cell Engineering/GMP Group.

View of the GMP facility of the Fraunhofer IZI.

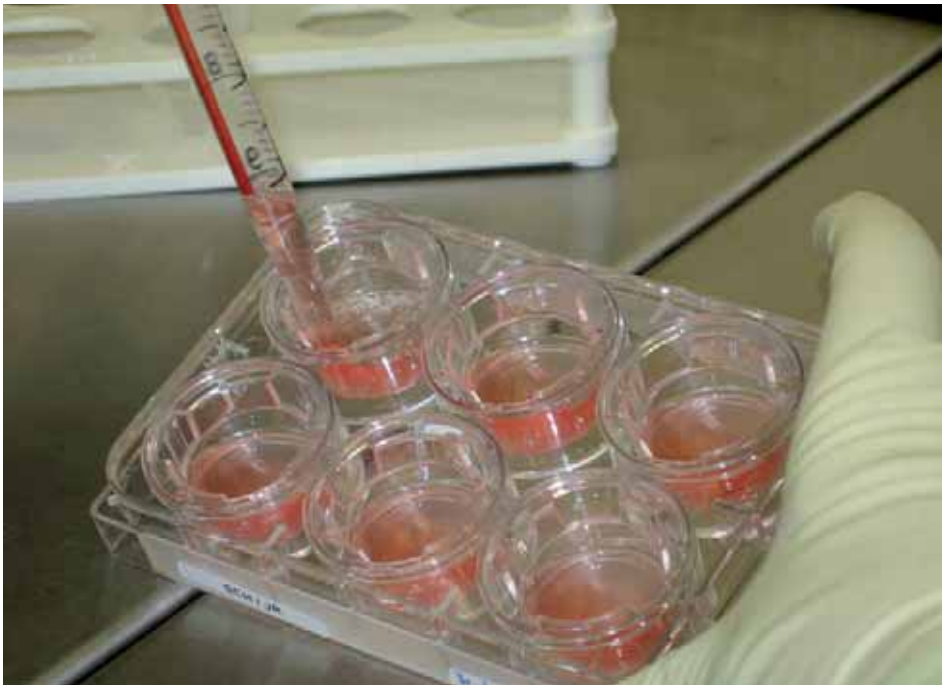
facilitate restarting stagnating tissue repair processes and achieving progress in wound treatment, in particular by persistent wounds. The market for this type of therapy has been estimated, according to recent studies, at 34,000 - 100,000 patients in Germany alone. EpiDex® is a cultured epidermal equivalent for the treatment of chronic wounds that is derived from patient cells from the outer root sheath (ORS). EpiDex® provides an alternative to mesh grafts, which require hospitalization, as it can be used on an outpatient basis. EpiDex® was developed by Prof. Hunziker in Switzerland and was successfully introduced into the market by the company euroderm GmbH, located in Leipzig.

Aims

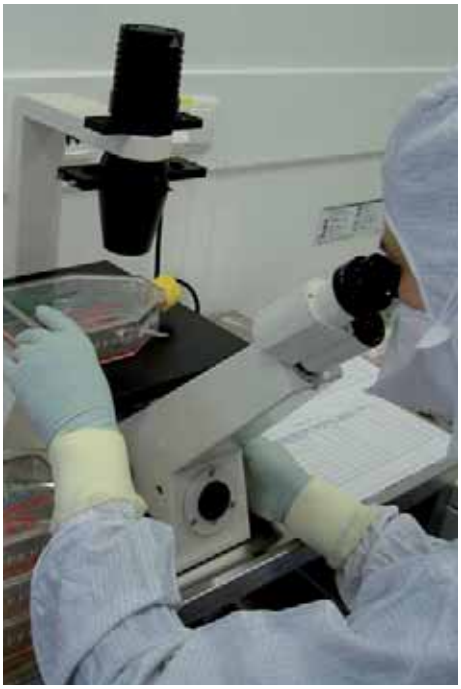
The complete pharmaceutical production of the autologous cell-based therapeutic EpiDex® had to be established, validated and finally officially approved by the German authorities at the central headquarters of euroderm GmbH in Leipzig. This process had to occur in the shortest possible timeframe. The goal of the project was to ensure the safe and reproducible production of EpiDex® for patient use in Germany and Switzerland as well as for the implementation of further clinical trials in anticipation of the marketing authorization from the European Medicines Agency (EMEA), which euroderm GmbH planned. Fraunhofer IZI's modern GMP clean room facility, with its design, equipment and staffing specifically specialized for production and quality control of such new therapy products, presented a suitable technological environment for a quick and high-quality, practical realization of these goals.

Results

First, the staff was trained and additionally necessary equipment was integrated into the facility and qualified, along with the clean rooms, according to the EC GMP Guidelines (Annex 15 EC GMP Guideline). Meanwhile, a revision of the quality assurance system was performed, followed by an alignment with the corresponding system at euroderm GmbH, as appropriate and necessary. After establishing these prerequisites, three validation batches of EpiDex® were manufactured, tested for quality and completely documented. The batch documentation for the validation batches, along with other materials, including documents describing the process, the rooms, and the personnel, was submitted in an extensive proposal for the manufacturing authorization according to the German Drug Act (§13 "Arzneimittelgesetz", AMG). After the proposal was reviewed by the "Regierungspräsidium Leipzig" and the higher federal authority, Paul Ehrlich Institute, a two-day GMP inspection took place. During this inspection, the clean rooms, the quality control lab as well as the



Production of EpiDex®.



Quality control.

documentation and quality assurance system were intensely examined. After the successful inspection, euroderm GmbH received the manufacturing authorization in the clean rooms of the Fraunhofer IZI, according to §13 of the German Drug Act (AMG). The authorization was received after a project time of only 6 months.

Potential

On the basis of the manufacturing authorization according to §13 of the AMG and with the assistance of the Fraunhofer IZI, euroderm GmbH can provide its innovative product, EpiDex®, to patients in Germany and Switzerland as well as pursue further official clinical trials in order to initiate the application for the European marketing authorization. The GMP Team of the Fraunhofer IZI has proven itself as a competent partner by the quick and successful GMP inspection of the pharmaceutical clean room facility, the quality control laboratory and the documentation and quality assurance system. This serves to recommend the GMP Team for future partnerships, particularly when one considers the speed with which the field of regenerative medicine is developing. A final benefit that helps to position the GMP Team is the extensive theoretical and practical trainings provided by euroderm GmbH. These trainings extended the know-how of the GMP personnel regarding the GMP-compliant manufacturing of modern cell therapeutic agents, in particular with respect to adult stem cells.

Air lock to the clean room.

Working in the clean room.

Special Background

The EC GMP Guidelines for Medicinal Products for Human and Veterinary Use and its annexes describe the basis for GMP production of all pharmaceuticals, including cell-based therapeutics. Annex 1, "Manufacture of Sterile Medicinal Products," is of particular relevance to this project due to the aseptic production. Furthermore, the European Guidelines, 2004/23/EC, 2006/17/EC and 2006/86/EC provide an extensive overview of the particular requirements of this product group. The European Parliament's Regulation on advanced therapy medicinal products (regulation [EC] No. 1394/2007), which was published on December 10, 2007, is very significant. This regulation will lead to a far-reaching harmonization with regard to manufacturing, testing and marketing authorization of cell-based therapeutics. Besides the European requirements, one must also adhere to the national legislation, for example, the German Drug Act (AMG), the "Ordinance for the Manufacturing of Medicanal Products and Active Pharmaceutical Ingredients" (AMWHV) and the law on "Quality and Safety of Human Tissue and Cells" ("Gewebegesetz").

Cell Engineering/GLP Group

Products/Services

- development, production, purification, and conjugation of monoclonal or polyclonal antibodies
- expression proteomics studies (2D-GE, DIGE)
- immunotoxicity and neurotoxicity studies (GLP)
- development of immunoassays for research and diagnostics, generation of antigens (recombinant, native)
- preclinical therapy models for R&D purposes or preclinical evaluation

Competencies

- antibody production (monoclonal or polyclonal)
- proteomics
- immunotoxicology, neurotoxicology
- *in vitro* assay development, protocol development
- animal models (mouse: infections, chronic, inflamed intestinal diseases, chronic arthritides; dog (Beagle): blood product testing – GLP)

More services of the group can be found on pages 28, 29 and 31.

Selected Project: B-cell Bound Specific Antibodies as an Early Diagnostic Tool

Background

The early diagnosis of infectious diseases increases the therapeutic chances.

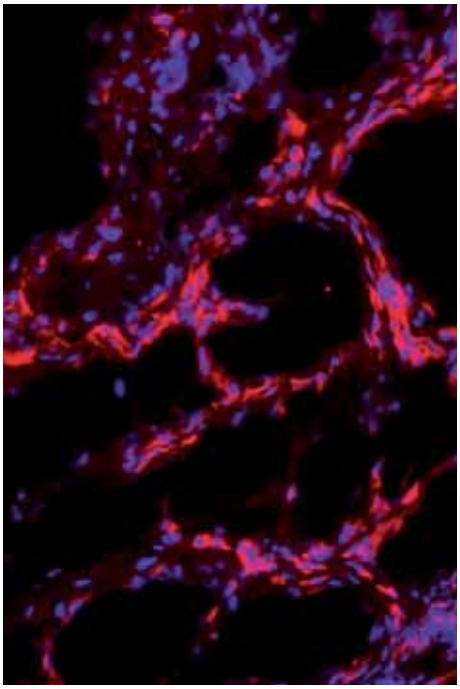
The production of specific antibodies by B-lymphocytes and the activation of antigen-specific T-cells are both sides of adaptive immunity. Antibodies secreted by activated B-cells, and finally differentiated plasma cells, accumulate in

Contact

Dr. Jörg Lehmann
Phone: +49 (0) 341/355 36-1205
joerg.lehmann@izi.fraunhofer.de

The group established a GLP laboratory for conducting immuno- and neurotoxicological GLP studies *(in vitro* or *in vivo)* or differential proteome analyses for industry. Another focus is the identification of novel biomarkers to be used in diagnostics or the therapy of chronic inflammatory or tumor diseases by using immunological, cell-biological and protein-biochemical approaches.

Cell Engineering/GLP Group (left to right): Ulrike Hoffmann, Ulrike Scholz, Ellen Svanidse, Birgit Ronneberger, Dr. Jens Knauer, Verena Veneruso, Dr. Peter Ruschpler, Dr. Jörg Lehmann, Christiane Füldner.



Immunocytochemistry: CD4-Cy3/RA synovial membrane.

the plasma and can be detected not earlier than day 5 post infection (p. i.; seroconversion) in plasma samples by appropriate diagnostic methods. During the early phase of an infection (i. e. day 1-4 p. i.), activated immature B-cells already synthesize specific antibodies, which are not yet detectable in the plasma. In contrast, those antibodies as well as antibody fragments can be detected intracellularly or in B-cell lysates by appropriate and sensitive methods. Thus, antibodies derived from currently activated B-cells that are produced early provide the opportunity to perform a novel antibody-based diagnostic test.

The aim of the project is to perform a proof-of-principle study by inducing specific antibodies in a well-standardized murine infection model (i. e. *Salmonella enterica* serovar Enteritidis) in order to compare their appearance in B-cell lysates or intracellularly in B-cells to plasma. The optimal method has to be identified.

Aims

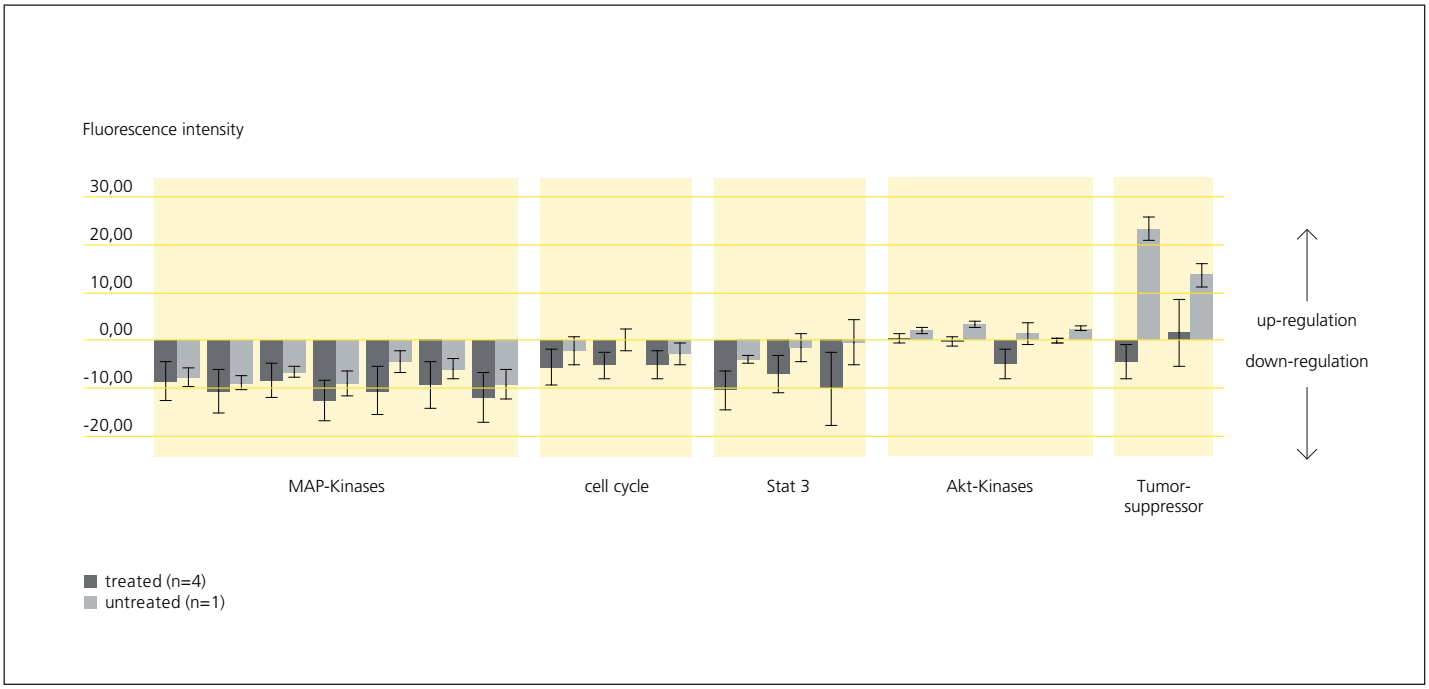
- establishment of an appropriate vaccination/infection model (i. e. recombinant *salmonella* flagellin/ *Salmonella* Enteritidis) to be used in the proof-of-principle study
- establishment of an appropriate and reliable method for the isolation of peripheral B-lymphocytes from vaccinated or infected mice
- detection of antigen-specific antibodies or antibody fragments in B-cell lysates or intracellularly in isolated B-lymphocytes derived from vaccinated or infected mice by using various diagnostic methods (i. e. ELISA, Western Blot, flow cytometry) – identification of the optimal method
- detailed characterization of the appearance and the time course (kinetics) of B-cell bound antibodies in comparison to free circulating plasma antibodies

Results

The first part of the project was completed, which comprised the experiments in the flagellin-immunization model. Intracellular antibodies (Ab) were analyzed via flow cytometry. Recombinant flagellin was marked with FITC. After B-cells were magnet-separated, the fluorescence labelled antigen was perforated using the paraformeldehyde/saponin method in order to detect B-cell associated Ab and Ab fragments. Furthermore, B-cell associated Ab and Ab fragments were analyzed from the lysate of magnet-separated B-cells using Western Blot and ELISA. Plasma was similarly examined.

All methods used in these experiments were validated with appropriate positive and negative controls.

The experiments have shown that following immunization with flagellin, antigen-specific IgM and IgG antibodies were induced and could be detected in serum after day 5 p. i..



Analysis of cellular signal molecules by protein micro-array: Comparison of treated and untreated patients on cellular signal molecule levels (normalized against controls).

Specific antibodies were detected via Western Blot on day 12 p. i. in cell lysates from isolated B-cells. Intracellular antibodies have not yet been detected by flow cytometry.

Potential

In the currently running second project part, we are attempting to verify Ab and Ab-fragments in a standardized mouse infection model (*Salmonella* Enteritidis). Thereby salmonella antigen-specific Ab will be verified by the above listed methods.

It will be critical for the diagnostic use of the method to determine at which frequence specifically activated B-cells can provide verification of diagnostically relevant B-cell associated Ab's.

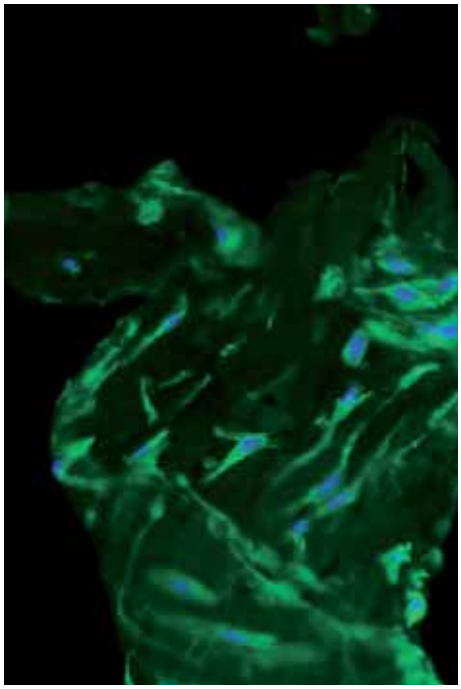
In order to answer these questions, we will proceed in two parts. Firstly, the primary immune response after a first infection of a mouse with an avirulent salmonella line will be analyzed. Later, we will examine the significantly stronger secondary immune answer after a repeat-infection with a virulent salmonella line.

Should these proof-of-principle studies show the success of the new diagnostic method, then the concept can be tested in other models – of particular interest will be viral infection models.

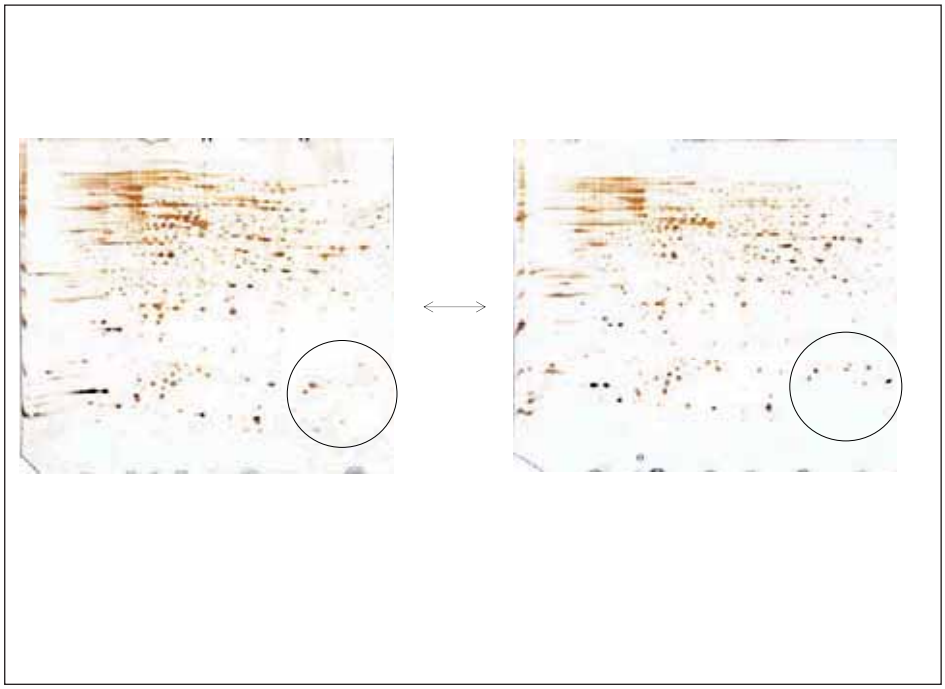
The most significant advantage of this new diagnostic method is the potential shortening of the diagnostic timeframe which under certain circumstances could be life-saving; in other words, re-establishing the time point at which an infectious disease unambiguously can be diagnosed. This should be particularly meaningful for a great number of dangerous viral infections.

Further Projects

- identification of novel biomarkers for chronic inflammatory bowel diseases
- inhibition of the NOD receptor signal pathway via inhibition on the kinase RICK – a potentially new therapeutic principle in SIRS and sepsis in a murine model
- definition of cell surface markers for the molecular imaging of rheumatoid arthritis
- preclinical study to evaluate the effect of UVC radiation on canine platelet concentrates



Immunocytochemistry: CD29-FITC/RA synovial membrane.



Expression proteomics: Massive parallel study of highly heterogeneous protein mixtures by 2D electrophoresis and mass spectrometry.

- biosystem steering technology for mesenchymal stem cell-based joint repair – adaptation of relevant methods to GLP/GMP-conform conditions
- development of a non-invasive test system for the early diagnosis of lung cancer via the detection of specific biomarkers in the breath condensate

Special Background

In May 2006, the new ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) Guidelines S8 "Immunotoxicity studies for human pharmaceuticals" (CHMP/167235/2004) of EMEA (European Medicines Agency) were internationally enacted. These guidelines require comprehensive immunotoxicological testing of all new pharmaceutical developments, in order to estimate potential adverse effects on the immune system as early as the development stage of the new products. Both immune suppressing and immune stimulating effects are included as of interest in the guidelines, as they both can disrupt the homeostasis of the immune system. While immune suppressive influences from pharmaceuticals can lead to restricted immune competence when faced with infectious pathogens or tumor cells, immune stimulating characteristics foster, potentially, the development of autoimmune diseases or allergies. It is expected that the immunotoxological examinations will be carried out under GLP conditions. Nonetheless, it is accepted that certain special test methods potentially will not meet the full GLP requirements.

The test methods recommended in the ICH-S8 guidelines comprise both *in vitro* and *in vivo* methods. An appropriate battery of tests is currently being established under GLP conditions in Fraunhofer IZI.

Furthermore, in May 2008, we are expecting certification as a GLP conform testing location for the analysis on adverse effects on the proteome of immune cells.

Immunological Models Group

Products/Services

- analysis of hematopoietic and mesenchymal stem cell potential of cells
- cell population of surfaces using adult stem cells and derived progenitors (tissue engineering)
- *in vitro*/*in vivo* proof of harmlessness of carrier material of scaffold or drugs on stem cells and immune cells
- biocompatibility/tolerance experiments in animal models (immune competent mouse) with a focus on hemato- and immunotoxicity effects
- quality control of cells and cell products in stem cell assays and cell function tests

Competencies

- *in vitro*/*in vivo* characterization of hematopoietic stem cells
- *in vitro*/*in vivo* characterization of mesenchymal stem cells including immunomodulatory properties
- human hematopoietic recovery in mice

More services of the group can be found on pages 28, 29 and 30.

Selected Project: Comparable Phenotypic and Immunologic Characterization of Adult Stem Cells

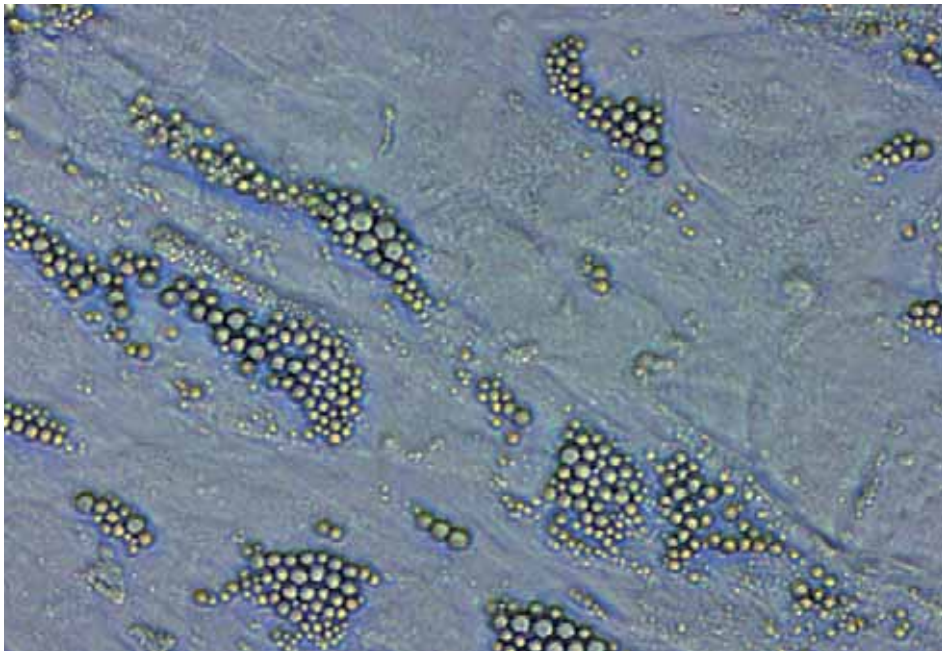
Background

Regenerative therapies are based on the enormous functional plasticity of stem cells. In the clinic, classic stem cell sources are currently being used like bone marrow, peripheral blood and umbilical cord blood that contain a small portion of hematopoietic and mesenchymal stem cells. The extraction of these cells for regenerative therapies is either associated with a high level of operative time and effort (as by bone marrow or peripheral blood) or

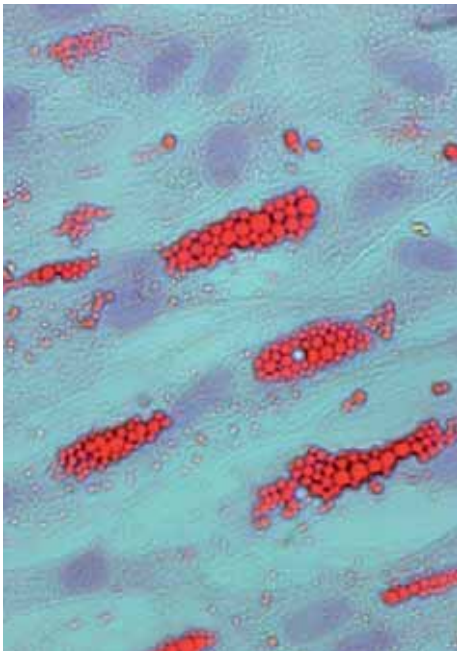
This group is focused on the isolation, cultivation and the phenotypical and functional characterization of mesenchymal and hematopoietic stem cells for the development of regenerative therapies. Based on the formation of functional human immunocompetent cells in a mouse model, the development of disease models and therapy processes are being pursued in cooperation with the University of Leipzig.

Contact

Dr. Manja Kamprad
Phone: +49 (0) 341/97 25-830
manja.kamprad@izi.fraunhofer.de



Phase contrast image of unstained cells during the development of fat cells from mesenchymal cells.



Adipocytes with red stained fat enclosures; the cell nucleus is shown in blue.

is restricted by being possible only at one time and often providing insufficient cell numbers (as by umbilical cord blood). Furthermore, the question remains to be considered, if the cells will display age-dependent changes with respect to the tissue sources that might impact the long-term success of a therapy. For these reasons, it is of particular interest to develop and test additional ethically acceptable tissue sources that might provide tissue-embedded, primary cells that display stem cell characteristics.

Aims

Mesenchymal stem cells exhibit clinically relevant immune modulating characteristics in addition to their many-fold differentiation capacity. The ability of the cells to suppress allogen-induced T-cell proliferation is particularly interesting with regard to the treatment of GvH reactions after transplantation of allogeneic hematopoietic stem cells. In the context of one of this group's projects, stem cell preparations of an alternative source were analyzed for purity, mesenchymal potential, as well as immunogeneic and immunosuppressive characteristics in comparison to mesenchymal stem cells from bone marrow.

Results

The stem cell preparations demonstrated a high vitality. Extensive flow cytometric examinations confirmed the homogenous composition of the preparations. Phenotypically, the cells were comparable with bone marrow mesenchymal stem cells. Individual expression patterns of adhesion molecules showed dependence on the cell sources. Both the alternative stem cell preparations and the mesenchymal cells from bone marrow were evaluated to be immunologically inert; they induced no allogeneically triggered T-cell proliferation. It is remarkable that the immunosuppressive potential is dependent on the stem cell preparation. Distinct differences in the mesenchymal stem cell potential between the preparations were found via *in vitro* differentiation assays.

Vaccine Development Group

Products/Services
- research and development of DNA vaccines for veterinary medicine
- pilot development of DNA vaccines for human medicine
- development of viral and non-viral vectors
- research and development of anti-parasitic vaccines

Competencies
- platform technology for the development and validation of DNA vaccines
- for application in veterinary medicine (prophylactic and, species-dependent, also therapeutic)
- potential for the development of similar DNA vaccines for human medicine
- zoonosis research
- parasite research

More services of the group can be found on page 30.

WNV: West Nile Virus

Selected Project: West Nile Virus: Development of a Vaccine and a Diagnostic Test

Background
West Nile virus (WNV), first isolated in 1937 in Uganda's West Nile District, is a zoonotic neuropathogen which can cause encephalitis. This virus infects not only birds, horses and lots of other mammals but also humans. WNV is transmitted by mosquitoes. Birds evidently constitute the natural reservoir of WNV; mosquitoes then acquire the virus from infected birds when feeding on their blood. WNV is spread from endemic areas partly by birds migrat-

Contact
Dr. Sebastian Ulbert
(Head of Laboratory)
Phone: +49 (0) 341/355 36-2106
sebastian.ulbert@izi.fraunhofer.de

PD Dr. Matthias Giese (Head of Group)
matthias.giese@izi.fraunhofer.de

This group is developing marker vaccines for use in veterinary medicine. Primary activities include research on DNA vaccines against viral infections in pigs, horses and in pets. Additionally, in January 2007, an extensive project on West Nile virus began. The development of a human vaccine against this zoonotic virus is planned.

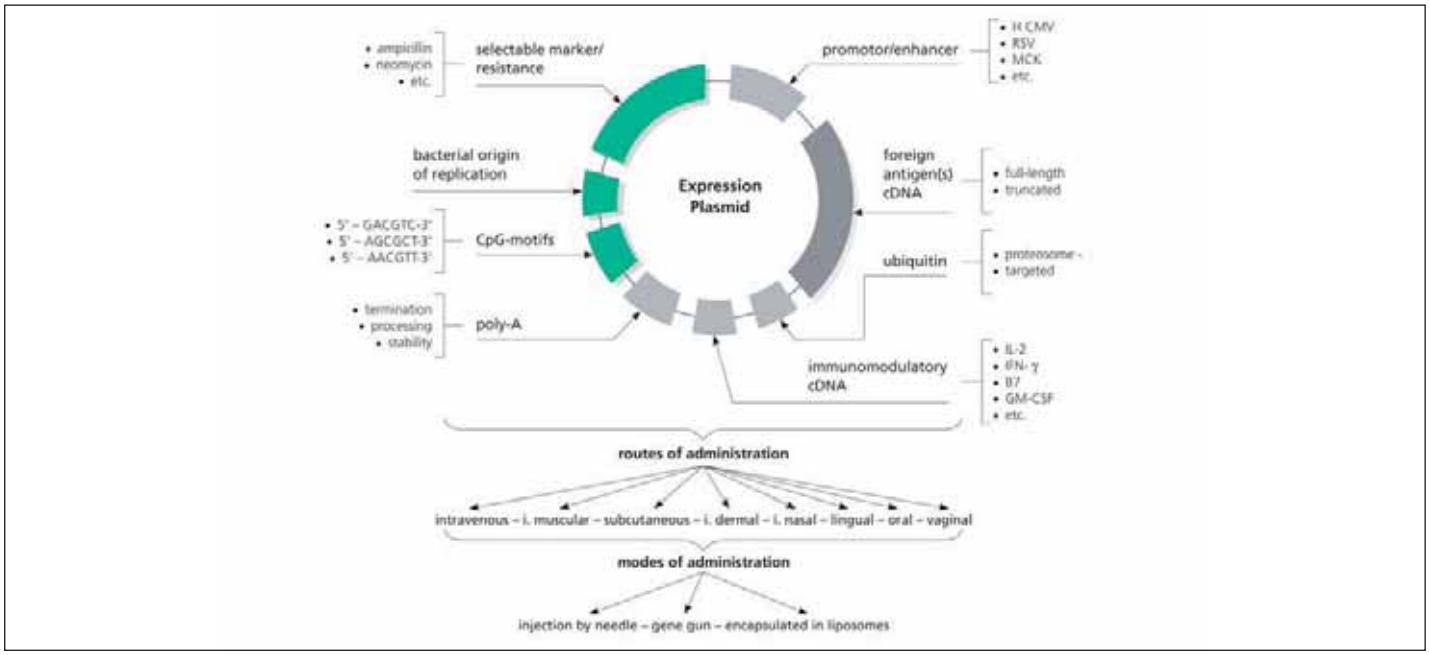


Diagram of an expression plasmid for DNA vaccination. The antigen is under the control of promoters/enhancers and the poly(A) sequence. The co-expression of various cytokines and ubiquitin contributes to immunomodulation. CpG motifs support the unspecific immune reaction and are part of the plasmid's bacterial backbone.

ing between Africa, Asia and Europe. WNV first broke out in the USA in 1999 and within a span of 5 years infected the entire North American continent. Numerous humans and animals were infected and a portion of the victims died. Following a drastic increase in the number of fatal WNV infections among humans in 2002 and 2003 in the USA (9,862 cases of the disease were recorded in 2003, of which 264 proved fatal), the number of people affected declined in 2004 and 2005. In contrast to the USA, almost nothing is known about the spread of WNV in Europe. Over the past few years, the virus has been detected in a number of European countries. According to a recent study, WNV has already reached the UK, probably being spread there by birds. In France, WNV has been observed since the year 2000, and was first detected in the Pyrénées-Orientales in 2006. However, no studies have been carried out into the prevalence of WNV in Germany. Moreover, so far no human vaccines against WNV have been developed anywhere in the world. As far as veterinary medicine is concerned, just one vaccine has been licensed for horses in North America, but there are no vaccines that can treat different species.

Aims

The objective of the project/program is to study the spread of WNV in Germany and to develop a vaccine that can be used on different species all over the world. A three-pronged approach has been adopted, comprising epidemiological studies on wild birds and horses, the establishment of a mouse infection model with diagnostic marker, and the development of a DNA vaccine, which will initially be tested on horses.

Results

During the last years, a DNA vaccine was successfully developed against a viral infection in horses (EAV/equine arteritis virus). This vaccine is not only being used in clinical studies prophylactically, but also for therapy of EAV-infected horses.

Potential

DNA vaccines are also referred to as third-generation vaccines. They are modern, highly efficient and biologically safe vaccines, which furthermore can also be produced inexpensively. GMP-conform production is possible at Fraunhofer IZI. First DNA vaccines are already registered for animals and in preparation for humans.

Special Background

DNA vaccination refers to the application of pure plasmid DNA in a eukaryotic expression vector in order to activate a complete immune response. This plasmid DNA bearing an antigen of the pathogen is usually applied intramuscularly, subcutaneously or intravenously, although oral administration is also effective.

Immune Tolerance Group

Products/Services
- development of cellular therapeutics and drugs for GvHD treatment
- development of antibody therapies, verification of pathomechanism
- testing of chemotherapy effects on organs and tissues
- intravenous, intraperitoneal application of cell grafts

Competencies
- experimental therapy models for xenogenic and allogeneic GvHD
- experimental cell culture models for testing of therapeutically relevant monoclonal antibodies
- chemotherapy in animals
- histology/immunohistology
- cell transplantation procedure in rodents
- production and analysis of histology slides (animal models)

GvHD: Graft versus Host Disease

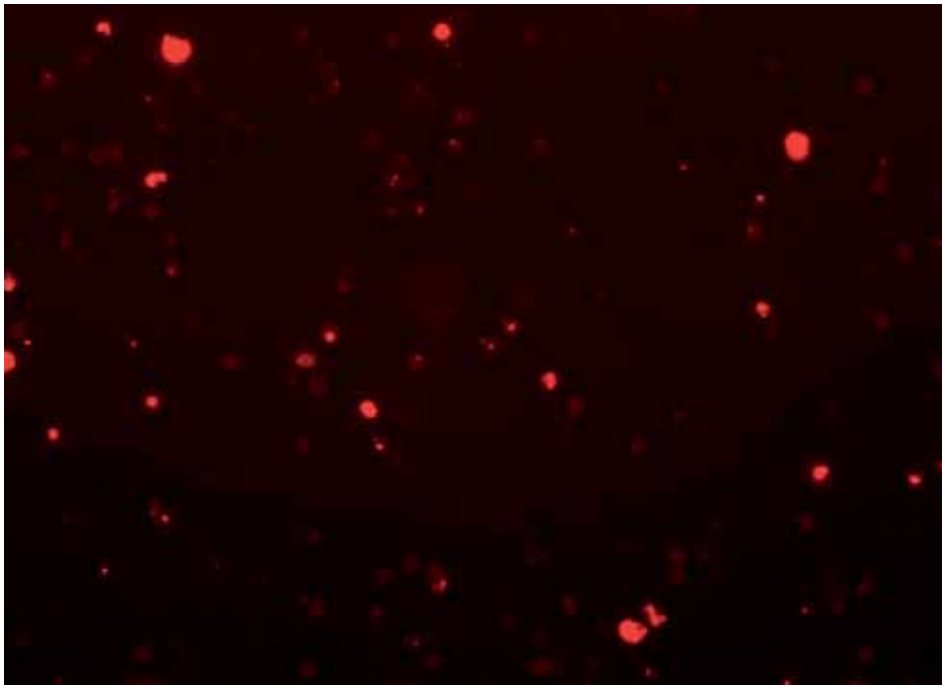
More services of the group can be found on pages 28-31.

Selected Project: Innovative Antibody and Cell Therapeutic Strategies in Stem Cell Transplantations

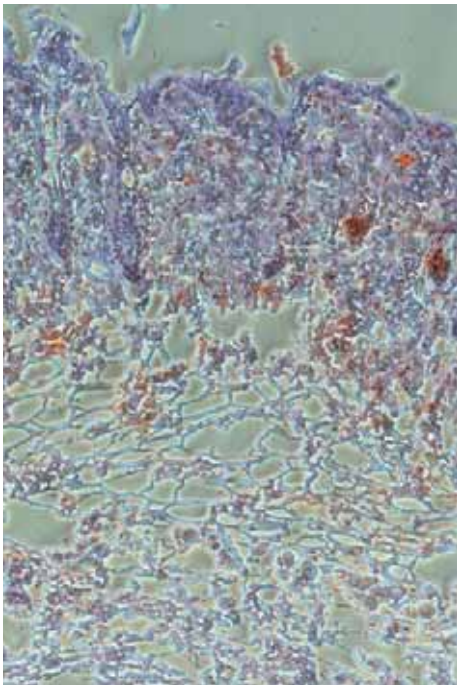
Background
Hematopoietic stem cell transplantations (world wide over 60,000 per year) are the only curative treatment option for many hematology-oncology patients. Despite remarkable successes with this therapy, patients are susceptible to many treatment-associated complications, besides the primary disease. Particularly infections, organ toxicity of chemotherapy, radiation or supportive therapy, as well as Graft versus Host

Contact
Dr. Stephan Fricke
Phone: +49 (0) 341/355 36-2205
stephan.fricke@izi.fraunhofer.de

This group's goal is the development of cell therapeutic and antibody based therapy strategies to treat complications after hematopoietic stem cell transplantations. New concepts of immunological tolerance with an orientation towards immunologic and therapy associated complications (e. g. GvHD) are being tested in new, institute developed animal models.



Fluorescence microscopic image of human CD4+ T-helper cells via Anti-CD4 antibodies. Own, therapeutically relevant antibodies were linked with fluorescent stains and the effect on T-helper cells was examined.



Immunohistologic image of human T-cells in the skin of transplanted, triple-transgenic mice.

Disease (GvHD), lead to significant problems.

Acute GvDH occurs in up to 78 percent of patients, chronically in 64 percent of all cases. In order to efficiently reduce the incidence of GvHD, stem cells must be transplanted that can renew the hematologic system with a quick regaining of immunological competence, demonstrate a high level of potential to repair organs, and tolerate the recipient tissue.

Current therapies (immunosuppressants) often need to be taken life-long, have many side effects and are only successful in a limited sense. Treating such complications cause significant costs (over 140,000 euros per patient).

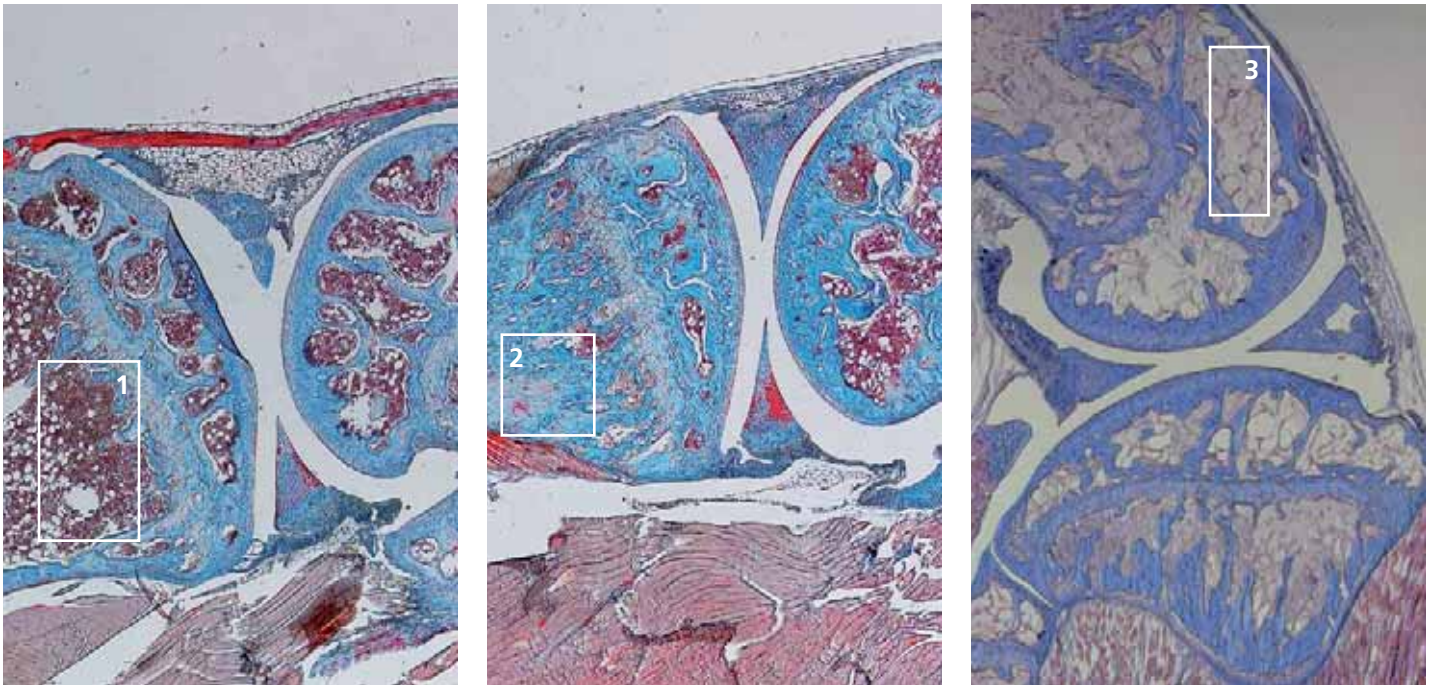
Aims

There is a pressing need for new therapies that will better control complications following stem cell transplantations. Such new therapies must be measured on the reduction or prevention of the associated complications. Using a human CD4+, murine CD4-, human DR+ transgenic mouse line, transplantation models are being developed for the preclinical testing of therapies. The triple-transgenic mouse expresses a human CD4 and MHC-II molecule while, at the same time, switching off the murine CD4 molecule. This makes it possible to simulate the interaction of human molecules in an animal model and to influence them therapeutically. Cell therapeutic strategies and induction treatments with anti-T-cell antibodies should lead to clinically applicable treatments.

Results

Using the triple-transgenic mouse line, we achieved the following results (*in vivo* and *in vitro*):

- the establishment of transplantation protocols for various stem cell fractions
- proof of the therapeutic influence of the applied grafts on the reconstitution of hematopoiesis and various organs without the occurrence of GvHD
- proof that some of the applied stem cell fractions demonstrate an advantage over standard treatments in an animal model
- the calculation of model functions that describe the conditioning therapy and the therapeutic efficiency of various stem cell fractions on hematological parameters in an animal model – first therapeutic effects of monoclonal anti-CD4-antibodies were shown based on acute and xenogenic GvHD models
- PCR-assays demonstrated and quantified transplanted cells (human/mouse) in different organs of the recipients



Histologic-morphologic aspect of different myelosuppressive radiation protocols (KAO-stains). After application of 3Gy in fractioned sessions, a weaker myelosuppressive effect is caused. In the bone marrow shafts, one finds hematopoietic islets more readily which indicates the regeneration of hematopoiesis (1). The application of 3 Gy leads to more extensive damage of the blood producing islets. The endpoint of complete autologous reconstitution will be reached later (2). After myeloablative chemotherapy and radiation, blood producing bone marrow is lost and is replaced with bone marrow fat cells (3).

– FACS protocols provided evidence of transplanted cells as well as chimeric analyses (human/mouse)
– proof of concentration-dependent therapeutic effect of a CD4 therapy on the activity of potential GvHD immune cells.

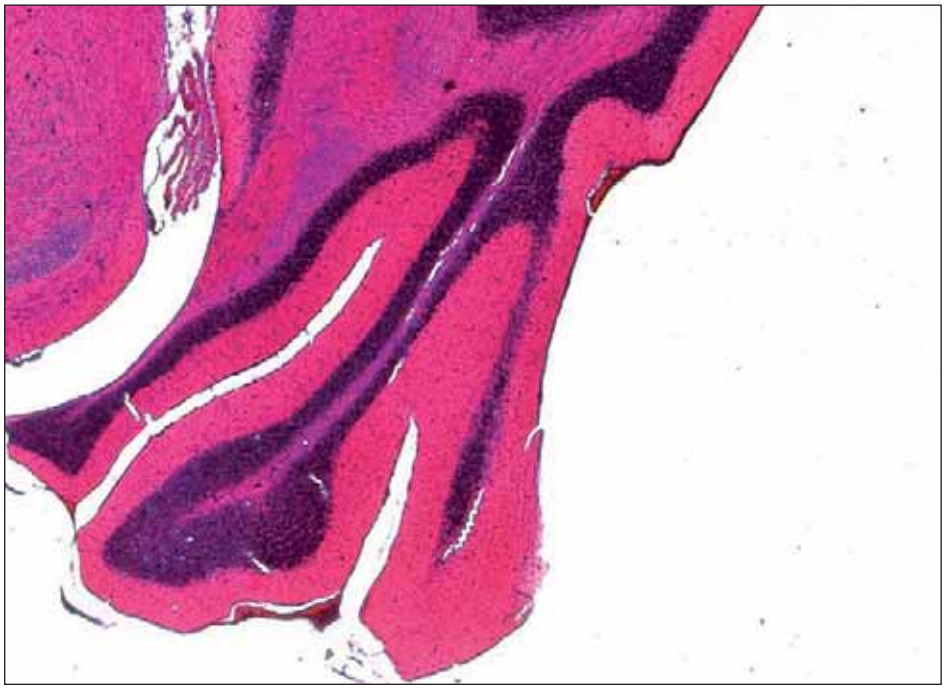
Potential

In the past decades, ever more sophisticated therapy strategies have been developed in hematology/oncology. The optimized therapies, however, have resulted in increased therapy associated short-, middle- and long-term complications. To control these complications, optimal techniques and applications still need to be developed, in order to improve patients' chances of recovery. Testing new therapies requires developing suitable *in vitro* and *in vivo* models, in order to bring promising treatments more quickly into clinical application. The presented results show that in a transgenic mouse model, the transplantation of various murine and human cell fractions is possible and that their therapeutic effect can be more precisely characterized. The used anti-CD4-antibody could be used as a therapeutic option in hematologic stem cell transplantations to control T-lymphocytes. Findings from this transplantation model could be used for further immunology and oncology based disease patterns that, for example, involve GvHD reactions.

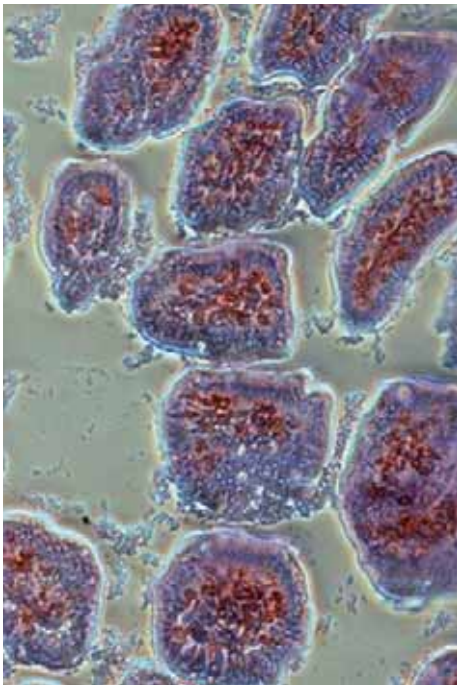
Special Background: Graft versus Host Disease

Graft versus Host Disease (GvHD) is the main complication after hematopoietic stem cell transplantations. T-lymphocytes contained in the graft react against the recipient's tissue and identify the host tissue as foreign. The process is comprised of multiple pathophysiologic levels.

By chemotherapy and radiation, pro-inflammatory cytokines are released and antigen-presenting cells (APCs) are activated in recipient tissue. These molecules and cells activate the T-cells contained in the graft, which release cytokines that recruit cytotoxic T-lymphocytes, monocytes, macrophages and natural killer cells.



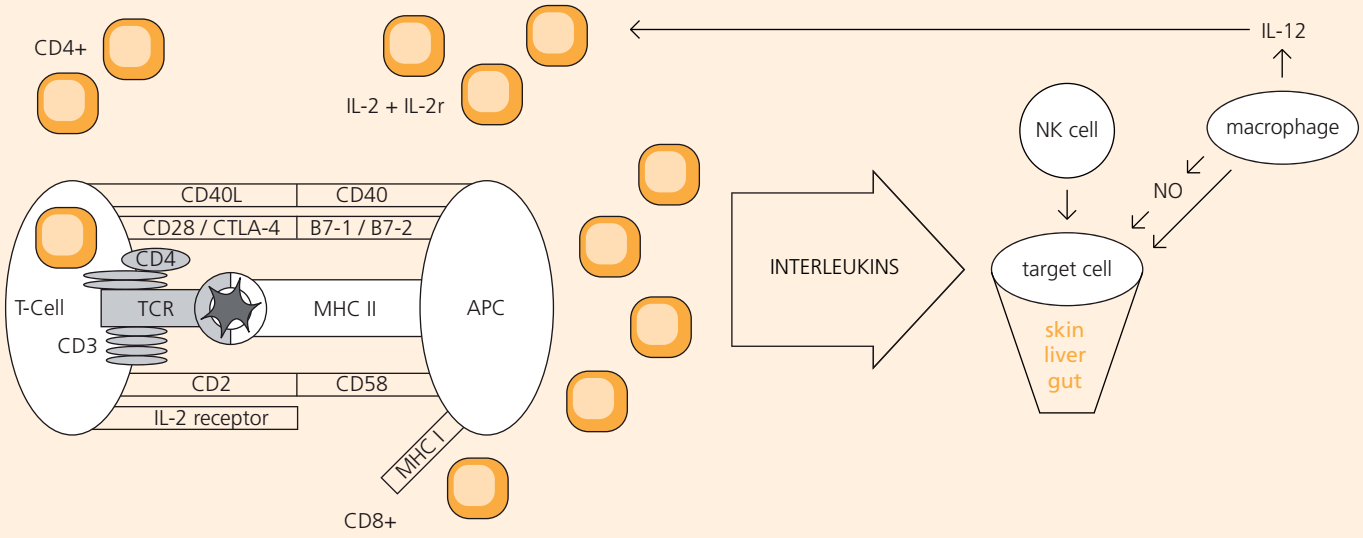
Histologic examination of brain tissue from triple-transgenic mice.



Immunohistologic image of human, peripheral, mononuclear cells in the intestine from transplanted, triple-transgenic mice.

Because of these effector cells and the continuous cytokine release, physiopathological processes are reciprocally stimulated by a positive feedback loop which together strengthen the GvHD. This establishes a systemic disease profile with specific effects on skin, liver, intestine and eyes.

A moderate form of GvHD can also be of benefit to the patient, because the T-lymphocytes of the graft can also destroy remaining tumor cells in the host (Graft versus Leukemia Effect).



Virus-Host-Interaction Group

Products/Services

- screening, development and analysis of antiviral vaccines and active agents
- development and testing of antiviral therapy concepts *in vitro* and *in vivo*
- screening of potential antiviral components (incl. identification of causal mechanisms)
- testing cells and tissues for biological safety
- examination of protein-protein and protein-cell interactions with state-of-the-art methods
- production of cell lines and expression systems for *in vitro* and *in vivo* studies
- production of standardized virus batches for transduction of various cell types

Competencies

- molecular mechanisms of retroviral infections, *in vitro* analysis of antiviral vaccines and active agents, verification of endogenous retrovirus activation, mutational analyses, molecular-biological, cell-biological, immunological and biochemical studies
- various cell culture systems for the examination of viral infections and their prevention, mucosal HIV transmission system, real-time-PCR quantification of intracellular retroviral components
- modulation of immune cells, *in vitro* differentiation of hematopoietic cells, flow cytometry, incl. the possibility of sorting under BL-2 conditions
- in cooperation with university partners, BL-3 safety laboratories are used
- viral and non-viral transduction of various cell systems

More services of the group can be found on pages 28-31.

Selected Project: Development of New Antiviral Strategies

Background

30-36 million people are infected worldwide with the Human Immunodeficiency Virus (HIV) and every year the numbers escalate dramatically; in comparison to 2003, the number has

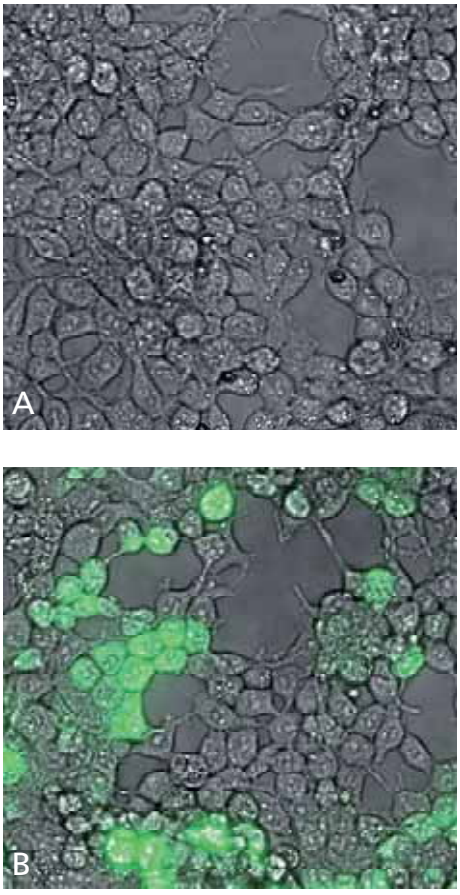
Contact

Dr. Jörg Baumann
Phone:
+49 (0) 341/355 36-2505
joerg.baumann@
izi.fraunhofer.de

Dr. Sabine Breun
Phone:
+49 (0) 341/355 36-2506
sabine.breun@
izi.fraunhofer.de

This group studies the interactions of virus and host using the example of HIV and other retroviruses. The focus is the development of new antiviral prevention and treatment strategies. To this end, we study the poorly understood mechanisms of innate intracellular defense against viral infections. Moreover, we aim to achieve a modulation of the immune response.

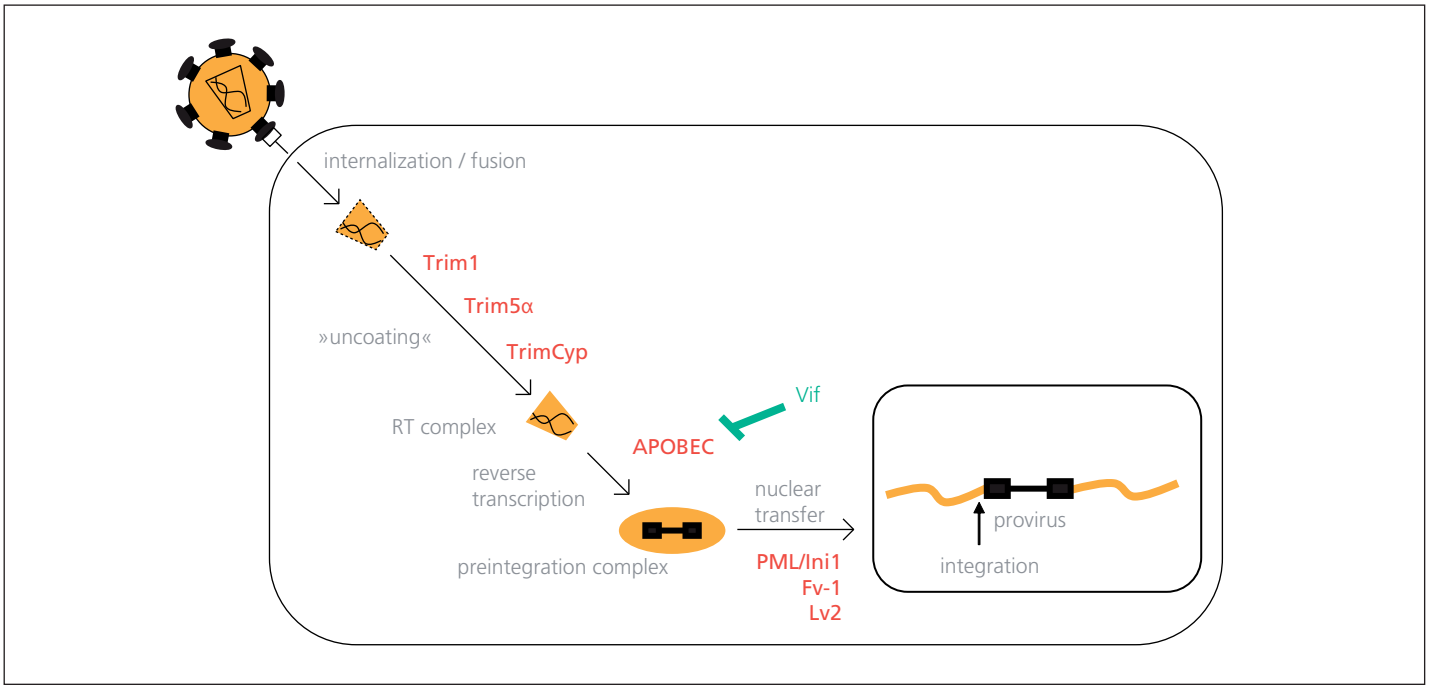
From left to right: Sidney Volger, Prof. Dr. Dieter Reißig, Dr. Sabine Breun, Solveig Tenckhoff, Kerstin Dunker, Jens Thomas, Florian Kirchheim and Dr. Jörg Baumann.



Detection of protein expression with fluorescence labeling: Human epithelial cells (A), light up green in fluorescence microscopy after transduction (B).

increased by 7 percent. More than 20 million people have died due to the acquired immunodeficiency syndrome (AIDS). Alone in 2007, 2.5 million people were infected with HIV. Licensed medicaments against HIV/AIDS attack four points in the viral life cycle: fusion of the virus particle with the cell membrane, reverse transcription of the viral genome, integration of the proviral DNA into the host genome and the maturation of the released particle to an infectious virion. Because of the high mutation and replication rate, it is only a matter of time until resistant virus populations develop.

The interaction of the virus with the host organism and its immune system is central to the research of this group at Fraunhofer IZI. Thus, we are able to obtain new findings about the immune response as well as the regulation of the immune system. Our goal is the development of new antiviral strategies and methods that will allow targeted modulation of the immune response.



Known intracellular restriction factors against retroviruses: In the framework of the innate immunity, restriction factors offer protection against retroviral infections by blocking the pathway of the virus inside the cell at multiple points. They restrict, for example, the uncoating or the release of the viral genome after penetrating the cell (Trim-proteins). Other factors cause hypermutation during reverse transcription of the retroviral genome into DNA (APOBEC). The viral protein, Vif, serves as a counterpart to APOBEC. If the generated viral DNA penetrates the nucleus of the infected cell, it will be integrated as a provirus into the cellular genome and thereby fixed in place. The transfer in the nucleus can also be inhibited by restriction factors (e. g. Fv-1). RT complex, reverse transcriptase complex.

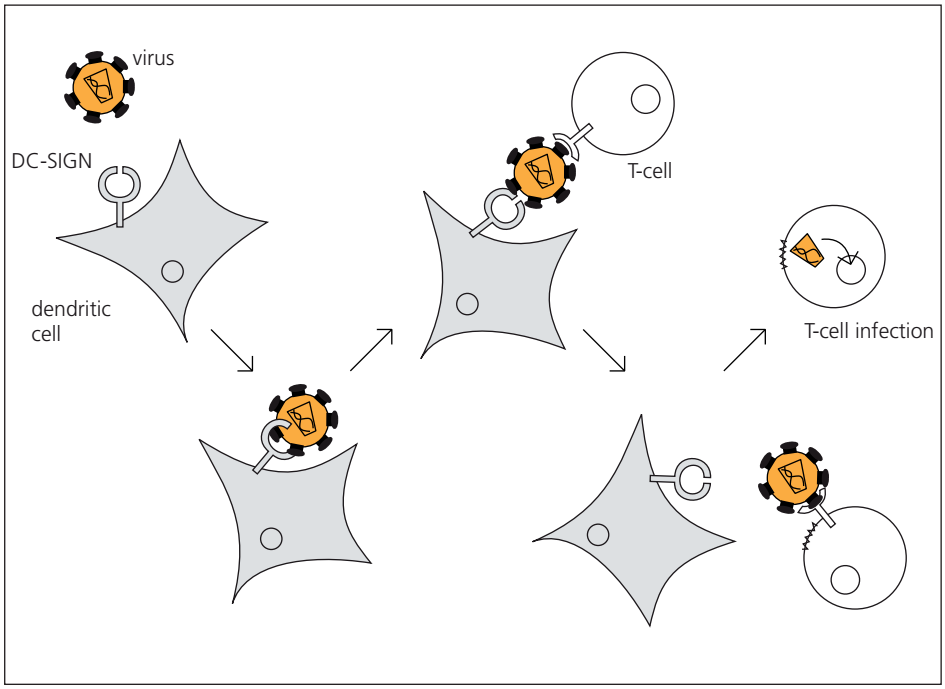
Aims

The group's start in Leipzig at Fraunhofer IZI last year brought current know-how from the National Cancer Institute in the USA to Germany. In the context of current research topics, cellular and viral systems and techniques, as well as domestic and international cooperations allow the group to develop new strategies against HIV/AIDS – all the way from basic research to application. In this effort, the Virus-Host-Interaction Group has set the following goals:

- isolation and characterization of as yet unknown co-factors for HIV; the identification of new resistance factors against HIV
- examination of the role of C-type lectins in the pathogenesis of HIV and other pathogens
- modulation of the immune response against pathogens and auto-antigens
- development of customized viral vector systems that transduce the most varied cell types *in vitro* and *in vivo*
- using nanotechnology in diagnostics and therapies

Results

The study of intracellular defense mechanisms against HIV has been extended to a genetic screening – a new experimental concept, with which Dr. Jörg Baumann and Dr. Sabine Breun were able to isolate an inhibitor of HIV replication from mice at the HIV Drug Resistance Program in the USA. Based on these results, the group developed strategies that block this intracellular path of the virus. Further resistance factors, that are active inside different cells against viral infections, are being isolated and characterized with molecular-biological, biochemical, cell biological and immunological methods. Their influence on viral replication is being studied and, if appropriate, modified. The reverse path is also being pursued by the group through the isolation of co-factors



Mucosal transmission of HIV (simplified illustration): HIV enters the organism via the mucosa. In peripheral tissue, immature dendritic cells are localized that express the receptor DC-SIGN. HIV binds to DC-SIGN and is "smuggled" by the dendritic cells into the lymph nodes. In the lymph node, the virus finds T-cells that express CD4 as well as co-receptors needed for a successful infection. The virus particles bound to DC-SIGN are presented to the T-cells. HIV interacts with the T-cells and now the virus can infect the T-cells very efficiently.

Viruses:
Retroviruses
(HIV-1, HIV-2, SIV, FIV)
Cytomegalovirus
Hepatitis B and C
Coronaviruses
Filoviruses (Ebola)
Dengue Virus
Alphaviruses
Measles Virus
West Nile Virus

Bacteria:
Mycobacterium tuberculosis
Helicobacter pylori
Streptococcus pneumoniae
Neisseria meningitidis

Protozoans:
Schistosoma mansoni
Leishmania amastigotes, pifanoi

Fungi:
Candida albicans
Aspergillus fumigatus
Ceratinophilic fungi

DC-SIGN, a C-type lectin on the surface of dendritic cells, binds a large number of pathogens. A selection of different pathogens that interact with DC-SIGN are shown.

that HIV requires for its replication. We are attempting to withhold essential cellular components from the virus and thereby stop its replication. This project is supported by funds from the European Union. A new platform has been developed using micro- and nanoparticles with which HIV infection and the development of drug-resistant virus strains can be observed. This project is financed through funds from the "Stiftung Industrieforschung".

Potential

Current antiviral strategies attack viruses directly. One serious disadvantage of strategies to date is the relatively fast development of resistance via the virus itself, as even just one mutation may have an influence on viral replication. In the future, modifying cells in the immune system will offer an important combination-potential with current therapy concepts. The group's goal to identify and characterize intracellular factors influencing virus replication opens the field to generate new therapy concepts. A new monitoring system is also being developed using nanotechnology to allow the therapy to be adapted accordingly.

The group continues to investigate the mechanism that is key for mucosal HIV transmission. The exploration of this mechanism is the basis for potentially preventing an HIV infection – this is conceivably more important than a therapy, as AIDS has been known for over 25 years and it remains incurable. As a part of the innate defense against pathogens, the identified factors are integrated into an extensive list of cellular and immunological processes. This makes them particularly interesting for questions that extend far beyond AIDS, for example, about the development and regulation of the immune system or to the pathogenesis of autoimmune diseases.

Immunotherapy – Oncology Group

Products/Services
- generation of specific cytotoxic cell lines (T-cells, dendritic cells, NK-cells, CIK)
- *in vivo* imaging of effector cells using BLI or fluorescence imaging
- sorting of effector cells for further investigation (cloning, *in vivo* testing)
- planning and development of clinical trials

Competencies
- expansion techniques for different effector cell systems including cytokine-induced killer cells (CIK) (human and murine)
- imaging facility, including bio-luminescence/fluorescence imaging
- cell sorting facility
- board certified doctor for internal medicine, hematology and oncology

CIK: cytokine-induced killer cells
NK: natural killer cells

More services of the group can be found on pages 28-31.

Selected Project: Generation and Characterization of Cytokine-induced Killer Cells (CIK) in Patients with Solid Tumors

Background
Metastatic cancer has a poor prognosis in general. For example, in patients with metastasized gastric or pancreatic carcinoma, the median survival range is between one to two years. Curative concepts are still not available. Chemo-therapy prolongs survival, but cannot cure patients, because of developing resistance against chemotherapy. Also, chemotherapy can induce severe complications like immunosuppression, fever, aplasia, nausea and loss of hair.

Contact
Dr. Christoph Schimmelpfennig
Phone: +49 (0) 341/355 36-3105
christoph.schimmelpfennig@izi.fraunhofer.de

The scientific focus of this group is on the development of new therapeutic strategies in the field of oncology/hematology. This includes either cell based immunologic approaches (use of multiple cellular effector systems) or non-immunological approaches (like nanotechnolgy).

Immunotherapy – Oncology Group (left to right): Dr. Anett Schmiedeknecht, Dr. Christoph Schimmelpfennig, Natalia Shurawel.

Imaging of luciferase-positive fibroblasts after intra-articular injection.

Therefore, new therapeutic strategies are highly warranted.

Immunotherapy is attractive, because it reinforces the immune system of the patient and gives him the opportunity to suppress the malignant disease.

Cytokine-induced killer cells (CIK) might represent a way of adoptive immunotherapy in patients with cancer. CIK cells are *ex vivo*-expanded lymphocytes that can be generated from murine splenocytes or human peripheral blood lymphocytes in the presence of γ IFN, IL2 and anti-CD3. CIK cells express the T-cell marker CD3 and also the NK cell marker CD16/CD56 or NK1.1.. These cells have a broad cytotoxicity against a variety of tumor cell lines. In animals, the injection of syngeneic or allogeneic CIK cells induces significant tumor reduction. In patients with Hodgkin's Lymphoma or Non-Hodgkin's Lymphoma, administration of autologous CIK cells induced tumor repression in some patients without causing toxicity.

Aims

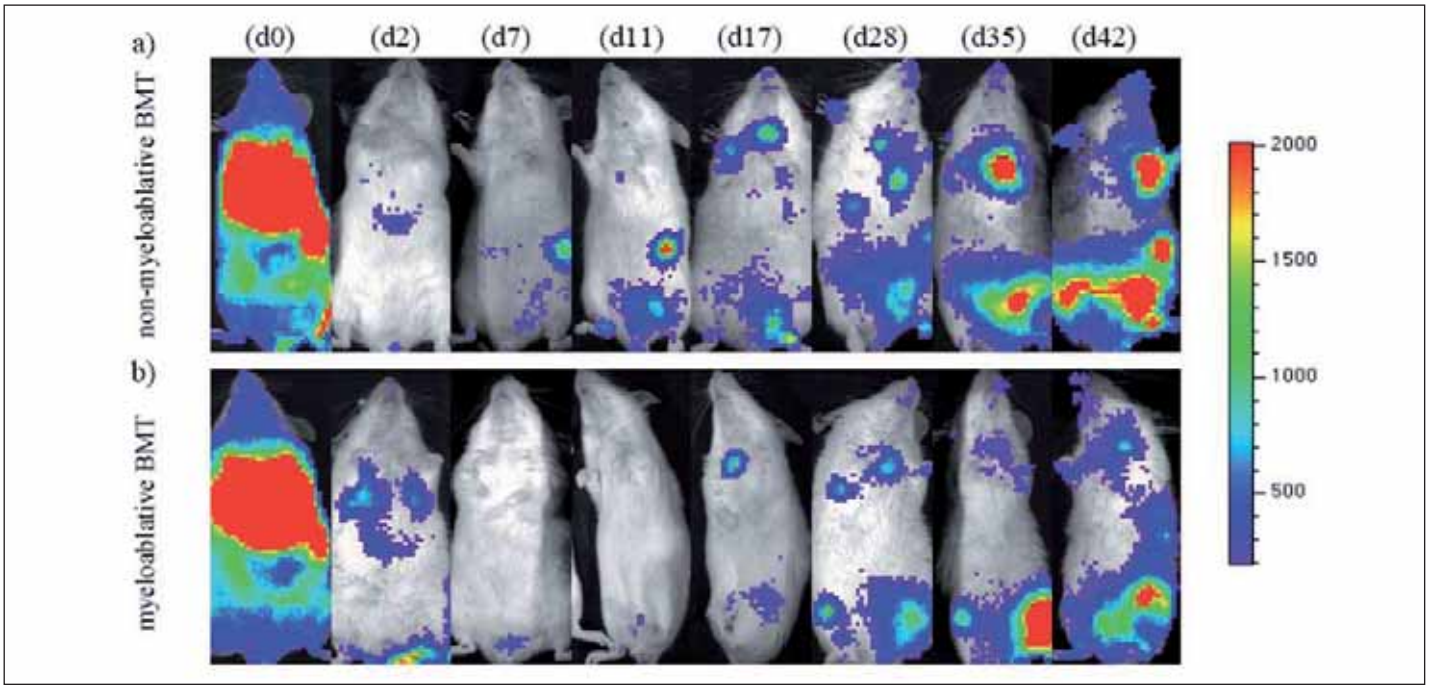
The group's aim is to refine and optimize the culturing technology of CIK cells for use in patients with solid tumors. This also includes further investigation of the biology of CIK cells in animal models with tumor diseases. Finally, we are planning to start a phase I/II clinical study in patients with solid tumors.

Results

Recently, it could be shown that CIK cells can be easily expanded from the blood of patients with gastric carcinoma and other malignant diseases. These cells expressed the typical immunophenotype of CIK cells and provided strong cytotoxity against a tumor cell line.

Potential

These characteristics seem to make CIK cells the ideal candidate for cellular therapy in patients with solid tumors. For this reason, we plan to extend and optimize our knowledge about the generation of CIK cells in patients with solid tumors. Our ultimate goal is to create an approved platform technology for cellular therapy. This technology allows the easy generation of CIK cells, which can be safely administered either alone or in combination with other therapies to any patient with a malignant solid tumor.

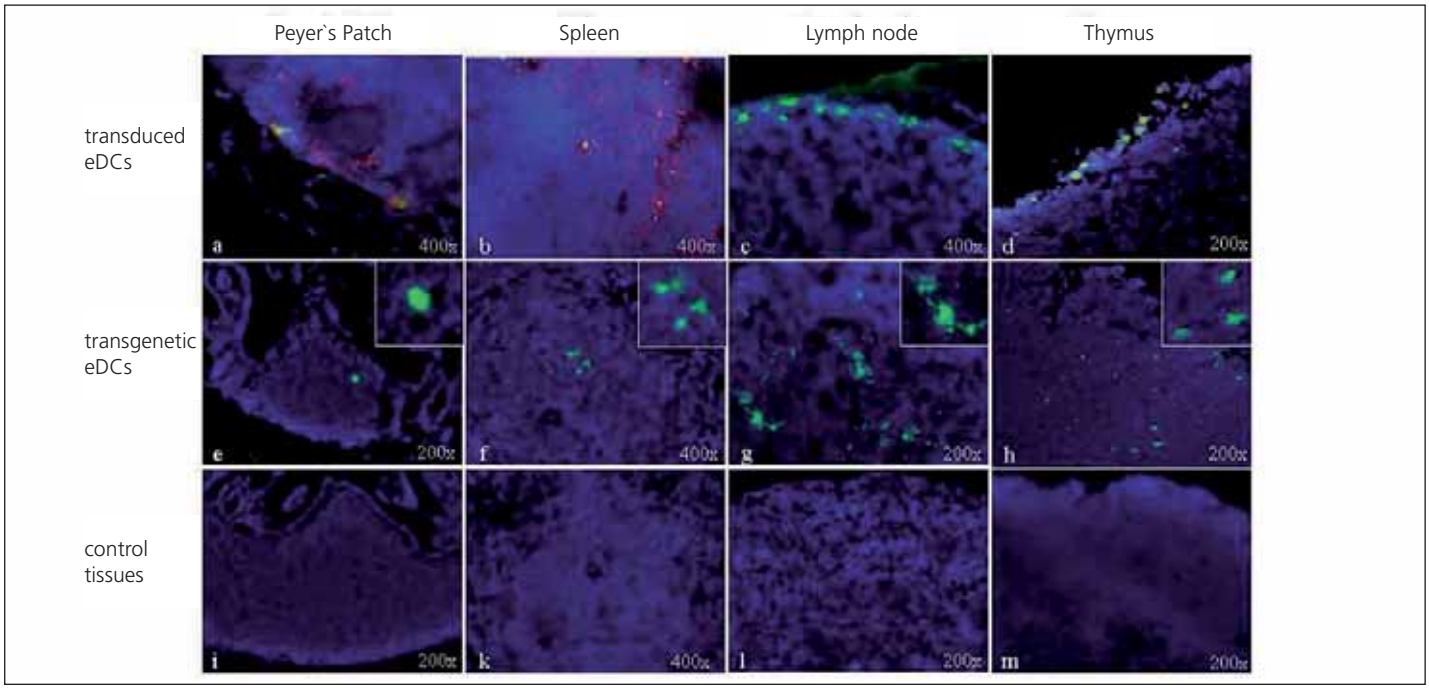


Migration of allogeneic *ex vivo*-expanded dendritic cells (eDCs) in bone marrow transplant recipient animals. The graphic shows the migration of allogeneic *ex vivo*-eDCs in bone marrow transplant recipient animals that were given either a non-myeloablative (a) or a myeloablative (b) bone marrow transplant. The elapsed time over 42 days in two representative animals is shown. In some animals, eDCs could be traced over 100 days with BLI.

Special Background

Little is known about the biology of CIK cells in patients with solid tumors. A major tool for investigating the biology of CIK cells in animal models is bioluminescence imaging (BLI), which is available at our institute.

BLI has proven to be a very sensitive technique for visualizing the migration and survival of cell populations in living animals. It allows the serial investigation of a single animal over an extended period of time and targeted histopathologic tissue sampling. BLI is based on the introduction of a reporter gene that encodes for the bioluminescent protein luciferase. The emission of bioluminescent light can be detected and the origin of the light source can be determined. In addition, multiple-function reporter genes like fluorochromes or luciferases from different species can link *in vivo* and *in vitro* assays. Therefore, BLI offers an important tool for refining and accelerating studies of cell fates and the function of different effector cell populations.



Verification of *ex vivo*-expanded donor-dendritic cells in various tissues after allogeneic transplantation in mice.

Stem Cell Technology Group

Products/Services
- *in vitro* assays for reproductive toxicology
- bioreactor process development (expansion/differentiation)
- development of cell culture media for stem cells
- biomaterial assessment (biocompatibility)
- pharmaceutical development and screening (bone/cartilage/heart/nerves)

Competencies
- *in vitro* screening models
- embryo toxicity and teratogenity
- susbstance testing under REACH
- bioreactor technologies
- technologies for embryonic and early stem cells
- signal transduction pathways and target gene activation
- reporter ES cell lines for target gene verification
- *in vivo* models for bone regeneration

More services of the group can be found on pages 28-31.

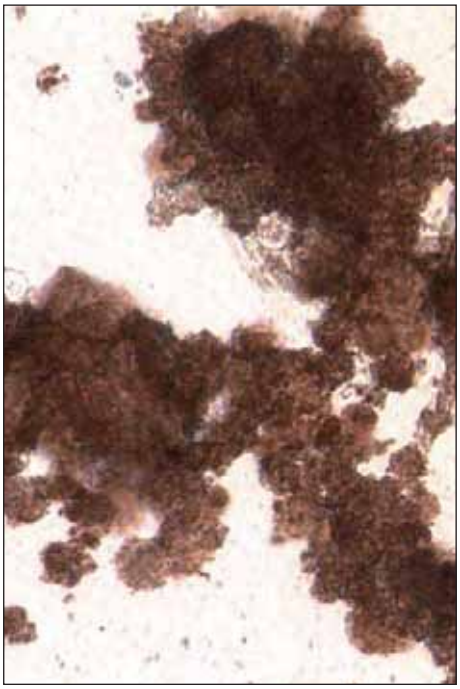
Selected Project:
Pluripotent Stem Cells in the Automated Prediction of Toxic Effects on Bone Development

Background
Birth defects are the leading cause of death of newborns. Congenital anomalies may be attributed to pharmaceuticals that are administered during pregnancy. The initial goal of early drug development programs is therefore to include animal studies to eliminate developmentally toxic side effects. To this end, existing *in vitro* tests are rarely

Contact
Dr. Nicole zur Nieden
Phone: +49 (0) 341/355 36-3305
nicole.zurnieden@izi.fraunhofer.de

Targeted intervention in complex events of tissue regeneration appeared to be technically infeasible for the past decades, yet novel insights have raised hopes to direct the potential of pluripotent stem cells for medical treatments and drug screening. The group develops high-throughput culture methods for stem cells and optimizes differentiation strategies into diverse mature cell types.

Stem Cell Technology Group (left to right): Susanne Trettner, Markus Zehe, Dr. Nicole zur Nieden, Dr. Vuk Savkovic, Huawen Ding, Alexander Seelinger, Beatrice Kuske, Dorota Kaniowska.



Von Kossa staining for mineralized calcium. Embryonal stem cells are differentiated to bone cells with vitamin D_3, vitamin C and a phosphate source. Matured bone cells are seen as brown/ black.

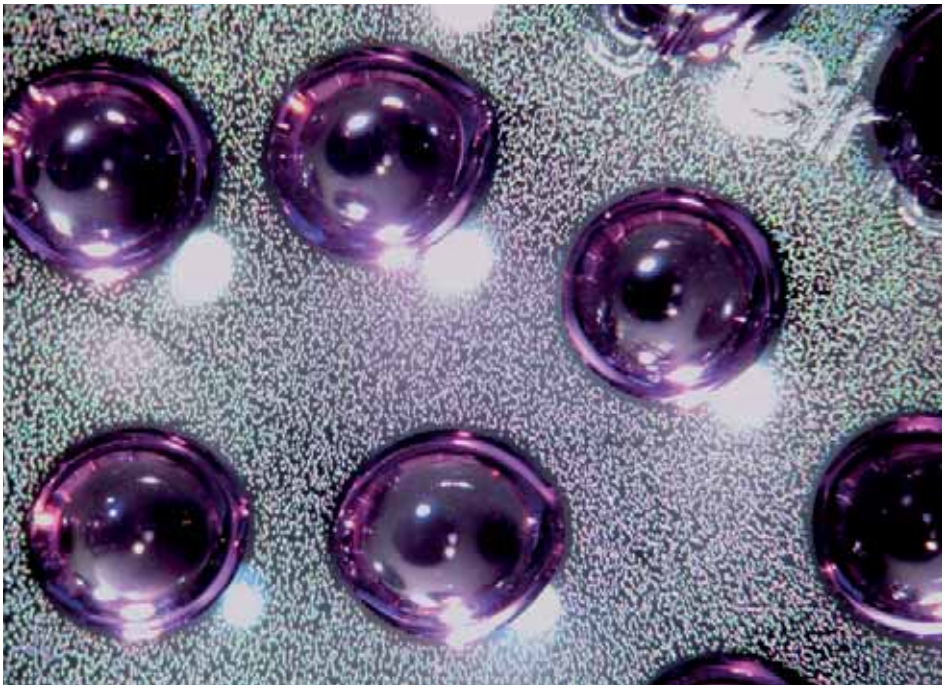
definitive as they show a low prediction potential and bring immense costs with them.

Due to their unlimited self-renewing potential and their multilineage differentiation potential, embryonic stem cells (ESCs) represent a potential endless source for preclinical screening of pharmaceuticals. ESCs are routinely used in industry in the context of the embryonic stem cell test (EST), which was evaluated to be superior to other known *in vitro* assays in an international validation study. However, one of the limitations of the EST is that it only evaluates one single endpoint (cardiomyogenesis) and the lack of a metabolising system and automation.

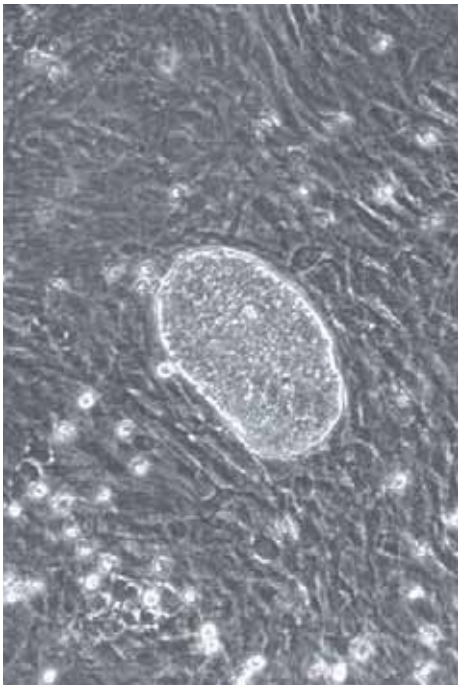
Aims

Approximately half of the current animal studies are conducted to evaluate the osteotoxic potential of new chemical entities. The goal of the research program is to provide the industry with a functional, automated *in vitro* osteotoxicity test that can routinely be used to screen compounds before they are introduced to the market or to evaluate existing ones.

The acceptance of an *in vitro* test in industry is dependent on three variables: the test must possess a high predictive potential, it must be inexpensive and it must have a short assay duration. Our group foresees the development of automated osteotoxicity models using ESCs for the prediction of bone development harming substances. This shall be accomplished by shortening the assay duration to raise commercial attractiveness and the use of a primate ESC line and human multilineage progenitor cells (MLPCs) to increase predictive power with minimal human handling.



Hanging drops. Mouse embryonic stem cells were stimulated to differentiate by the so-called hanging drop method. A single cell suspension is produced, which is pipetted as small drops on the cover of a petri dish. The cells contained in the drops condense to form cell aggregates at the bottom of the drops.



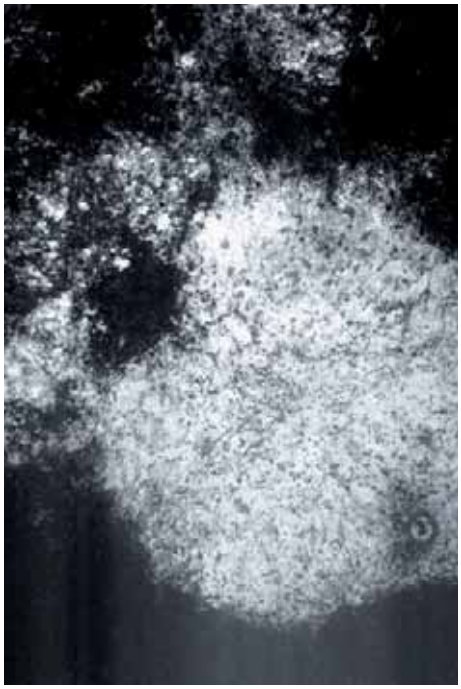
Embryonic stem cells from the common marmoset monkey *(Callithrix jacchus)* are kept in the pluripotent state on a so-called feeder layer of embryonic mouse fibroblasts with the addition of basic Fibroblast Growth Factor.

Results

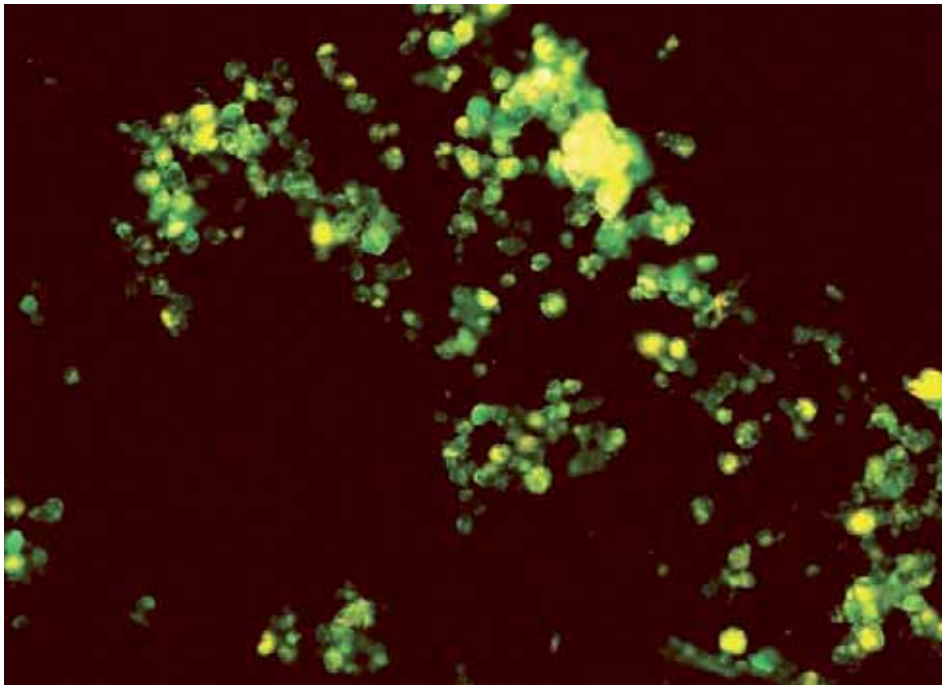
The group has several years of expertise in the area of directed differentiation of stem cells. Protocols for the directed differentiation into osteoblasts from murine ESCs were established a few years ago and now have been successfully transferred to primate ESCs in the first step of this project. Additionally, human multilineage progenitors generally also respond to differentiation induction using our standard protocols with initiation of osteogenesis. However, due to their longer population-doubling times and senescence in culture, it will be difficult to generate cells in adequate numbers and adequate time for the inoculation of bioreactor vessels. In the near future, studies will follow to enhance the differentiation efficiency further and characterize appropriate endpoints.

Potential

The introduction of new endpoints will lead to the shortening of the assay duration, whereby costs are lowered and the attractiveness of the assay for industry is raised. Based on the usage of primate cells, the predictive power of the test will further increase. The goal is to completely substitute *in vivo* osteotoxicity studies with the automated *in vitro* assay.



Phase contrast image. Embryonic stem cells are differentiated into bone cells under the influence of vitamin D_3. Mature, mineralized bone cells appear black in a light microscope without additional staining.



Tetracycline labeling. Embryonal stem cells were differentiated into bone cells using vitamin D_3, vitamin C and phosphate. When tetracycline is added to the culture medium, it is incorporated into the newly synthesized bone matrix. Exciting the cells with UV light causes the tetracycline to fluoresce; whereby the mineralized cells are visualized as yellowish cells.

Special Background

Definition of Stem Cells

All types of stem cells are described using two characteristics: their capacity for self-renewal and their differentiation potential.

Capacity for Self-Renewal
Stem cells have the potential to continually produce daughter cells that retain the same characteristics as the original cell. This daughter cell capacity occurs through asymmetric division, on the one hand daughter cells with stem cell properties and on the other hand differentiated daughter cells are produced.

Capacity for Differentiation into Specialized Cell Types
Stem cells are somatic cells that are not yet differentiated. This means that they are not yet in a form that specializes them for use in the organism.

Types of Stem Cells

Stem cells are primarily distinguished by their age and potential for differentiation: the ontogenetically earliest stem cells are the totipotent embryonal stem cells from which the primitive germ stem cells as well as the somatic stem and progenitor cells arise, which one finds in nearly all tissues of the adult body.

Stem Cell Biology Group

Products/Services

- aging tests (evaluating e. g. anti-oxidants, herbs, pluripotency inducers)
- technologies to "rejuvenate" cells, regenerative tissue culture
- testing of stem cell aging and pluripotency
- reprogramming of somatic cells to progenitor cells (iPS)
- development and optimization of new cryoconservation processes

Competencies

- aging research: evaluation of cell aging
- aging research: manipulation of cell aging
- stem cell biology
- reprogramming
- cryoconservation

iPS: induced pluripotent stem cells

More services of the group can be found on pages 28, 29 und 31.

Selected Project: Partial Reprogramming

Background

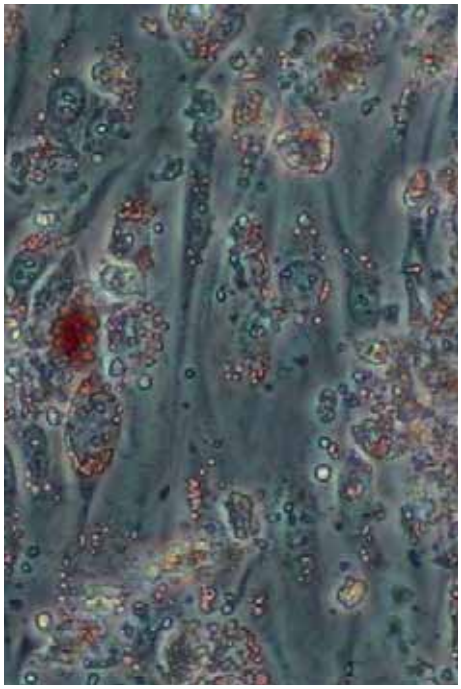
As stem cell science and tissue engineering technology mature, the availability of multipotent, readily available, immuno-neutral stem cells from an ethically uncontroversial source becomes more prominent. One promising venue lies in the reprogramming of mature body cells towards a multipotent state. All body cells derive from a totipotent, virtually immortal stem cell, and almost all body cells share the same genes

Contact

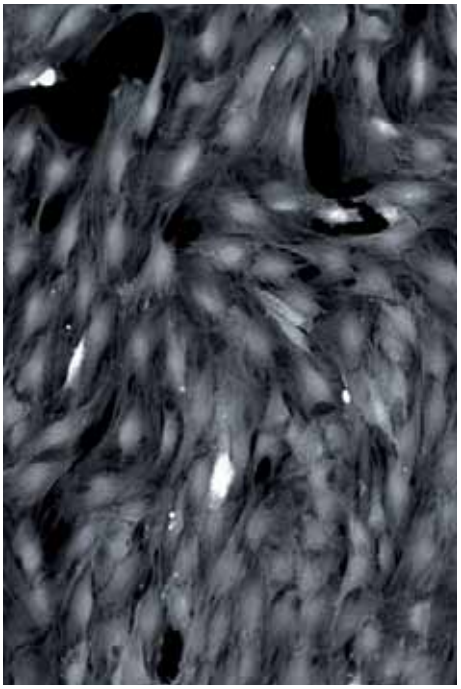
Dr. Alexandra Stolzing
Phone: +49 (0) 341/355 36-3405
alexandra.stolzing@izi.fraunhofer.de

The group 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.

Human pluripotent stem cells from bone marrow.



Human adipocytes (fat cells) from stem cells.



Human mesenchymal stem cells with stained actin-cytoskeleton.

with this ancestor. However, as cells differentiate, they become locked into a particular expression profile. The state of the DNA methylation and acetylation, ("epigenetic imprinting") is responsible for the gene activity required to maintain the expression profile underlying a differentiated phenotype. As epigenetic modifications do not alter the genetic blueprint, and the differentiated profile is plastic – potentially open to reversal and modification – this raises the possibility of "rejuvenating" a cell, turning a differentiated or old cell into an undifferentiated or proliferative cell.

Aims

In cooperation with Savita GmbH, the project aims to achieve robust reprogramming of adult body cells (fibroblasts, cardiomyocytes and astrocytes) without the aid of viral vectors towards a progenitor state and to evaluate the potential of these cells in cell therapy. We will use several age and pluripotency markers to evaluate the reprogramming effect and control the cell epigenetic status by measuring methylation patterns.

Results

Reprogramming is established and the first reprogrammed cells are being analyzed in terms of cell age and pluripotency. A special cell culture model was developed to maintain stem cells in a state of pluripotency or to reverse lost pluripotency.

Potential

The reprogramming of somatic body cells towards progenitor or stem cells opens up a new source of stem cells for cell based therapies. In cases where stem cells from a patient could be used or in cases where the stem cell pool is reduced due to aging, this method would be useful. As this method uses the patient´s own cells, no immunological risks are expected.

Neurorepair Group

Products/Services

- stepwise, cost and result orientated development and verification of cell therapies for stroke
- preclinical process development in large animals
- *in vivo* monitoring of neuronal regeneration
- analysis and description of cellular regeneration processes
- support and consulting services in the development of trials

Competencies

- multi-modal system for evaluation of cell therapies in relevant animal models
- unique large animal model for long-term evaluation of experimental stroke treatments
- application of modern imaging techniques, also in combination
- detailed histological and stereological tissue sample analysis
- close partnership with clinical stroke experts

More services of the group can be found on pages 28-31.

Selected Project: Autologous Cell Therapy of Stroke

Background

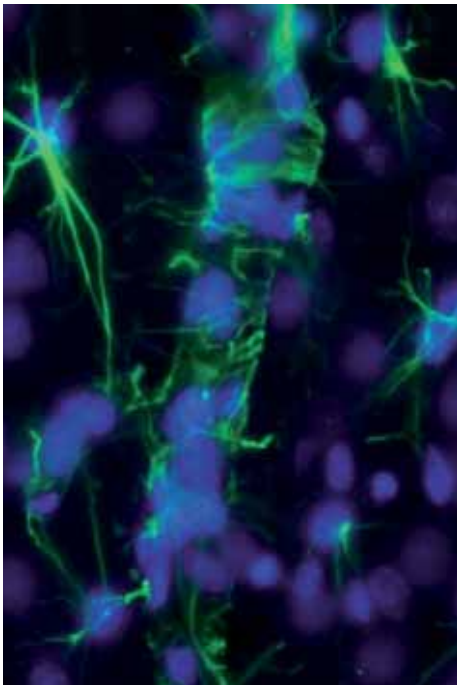
Ischemic stroke is the third most common cause of death in the western world and furthermore represents the most common reason for permanent disabilities in adulthood. Despite thrombolysis, there is actually no therapeutic approach for the successful treatment of stroke that aims at its pathophysiological causes. Furthermore, the protocol for thrombolysis is severely limited by

Contact

Johannes Boltze
Phone: +49 (0) 341/97 25-820
johannes.boltze@izi.fraunhofer.de

The group focuses on the development of novel therapeutic approaches for ischemic stroke based on non-embryonic stem cells. Next to cell culture experiments, specialized small and large animal models are used for behavioral and histological evaluation. Sophisticated imaging techniques (MRI/PET) allow the *in vivo* monitoring of regeneration. Furthermore, the group investigates the genetic background of dyslexia.

Neurorepair Group.



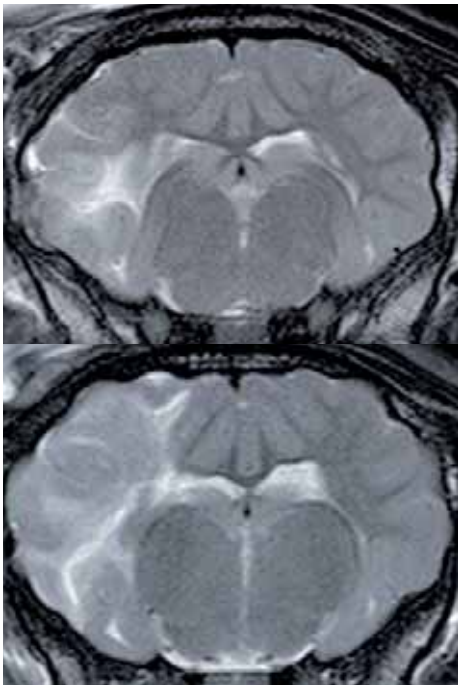
Reactive astrocytes after stroke in rat brain. Astrocyte processes cover a brain capillary that can be identified in the centre of the image. Blue: DAPI (nuclear staining).

a narrow time window of 3 to 4.5 hours, which restricts application of the protocol to less than 10 percent of all stroke victims even in well-developed areas. This is even more problematic if one realizes that therapeutic efficacy drops dramatically within the progression of the time window. Any attempts to extend this narrow time window have failed and the rate of therapy-caused complications rises significantly at later time points. Therefore, there is an urgent need for novel therapeutic concepts, for example based on stem cells.

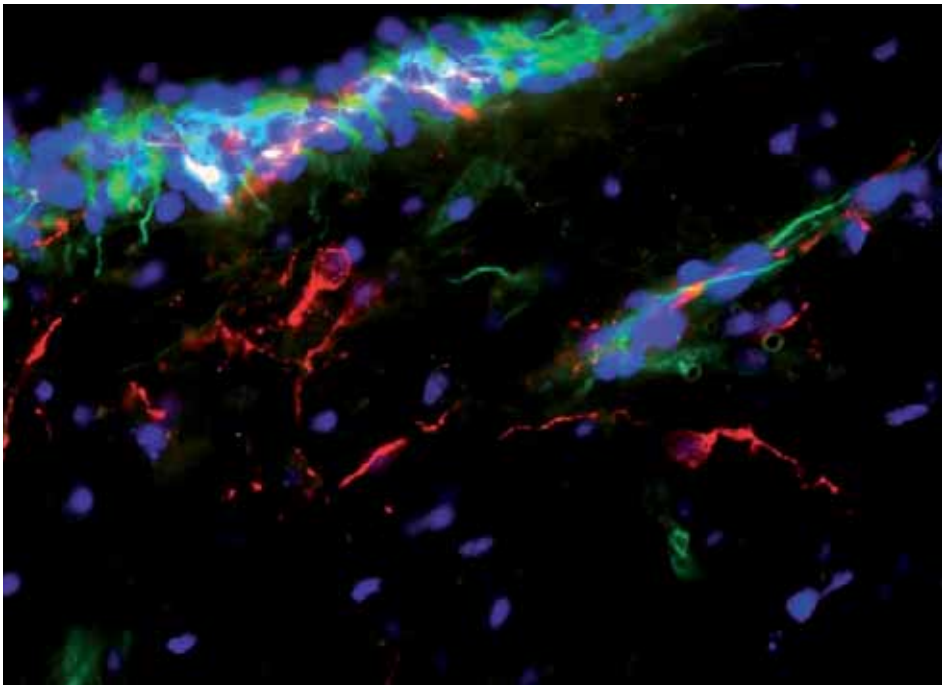
Aims

The Neurorepair Group, together with its partners, aims to develop a novel, autologous cell therapy for stroke and finally to transform the approach into a clinically applicable protocol. Subsequent to an efficacy screening *in vitro* as well as in common small animal models of stroke, the long-term evaluation of the concept in a unique large animal model, developed in the group, was needed. This is of special importance, because all therapeutic approaches based on neuroprotective substances showed good results in rodent models, but failed in clinical trials so far. Accompanying behavioral phenotyping and immunohistochemical brain specimen analysis, sophisticated imaging techniques including MRI and PET should be used in the evaluation of the therapeutic approach. Finally, the concept had to be translated into a protocol for a clinical phase IIa/b trial.

The entire experimental setup had to be designed in such a way that the application of any other cell product or neuroprotective agent, that may be, for example, provided by partners, could be tested and compared to the existing results using the already developed protocol.



Focal ischemic lesion in ovine brain, 24 hours after occlusion of the middle cerebral artery. (upper panel: slight ischemic lesion, lower panel: moderate ischemic lesion, indicated by diffusion disturbance).



Migrating neural progenitor cells in the rodent subventricular zone. Red: double cortin (labels migrating neural stem and progenitor cells); green: nestin (marker for stem and progenitor cells); blue: DAPI (nuclear staining).

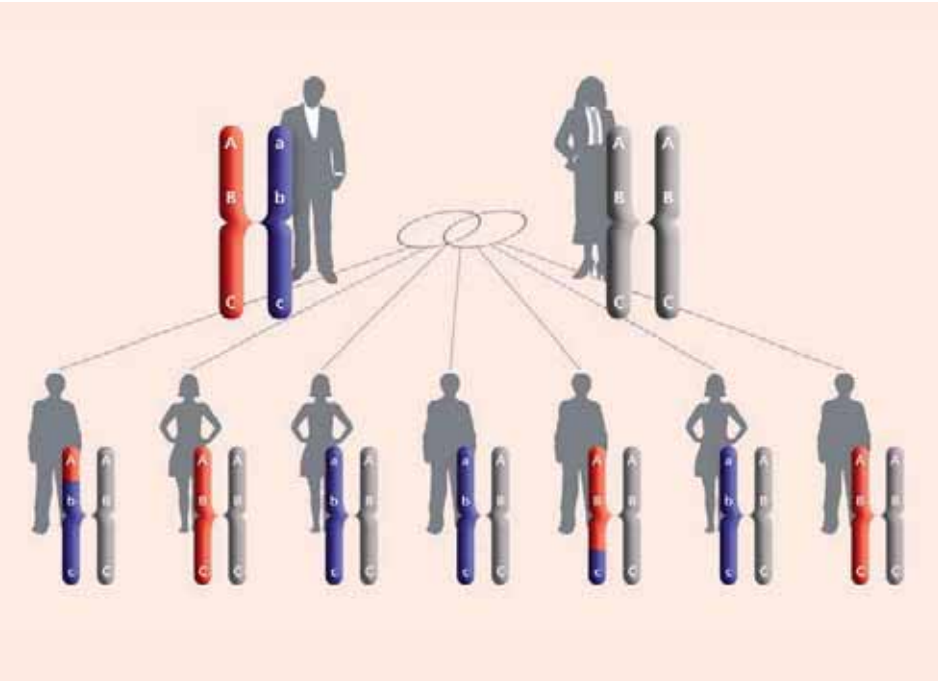
Results

The stem cell containing mononuclear fraction of human cord blood and bone marrow showed a prominent neuroprotective capacity *in vitro*. Following neuronal hypoxia, the ratio of apoptotic neurons in cell culture was reduced from 80 percent (controls) to an average of 20 percent. These results could be confirmed in small animal trials: there was a significant reduction of the stroke lesion volume and a clear motoric and sensoric improvement after application of both cell populations. Because only bone marrow can be used as a source of autologous stem cells for a significant number of patients in the near future and as it has also shown promising results after treatment of acute myocardial infarction in humans, the efficacy of autologous bone marrow transplantation was investigated in sheep. Again, there was a significant reduction of behavioral deficits in treated subjects as well as a cell concentration dependent reduction of the lesion size that was evident in MRI, PET and neuropathological investigations. Based on these findings, a protocol for a clinical phase IIa/b trial was designed.

Potential

Final experiments to prove the cell therapeutic principle are being performed in our group. In parallel, a consortium for an upcoming clinical trial was founded together with clinical partners from stroke units in Germany. After approval of the trial by the ethics commissions and the development of a GMP-conform production protocol for autologous bone marrow mononuclear cell samples (supervised by the Paul Ehrlich Institute) the clinical trial will be performed hopefully in 2009.

Rat in 1.5 T MRI scanner.



The Neurorepair Group investigates possible genetic basics of dyslexia. Early diagnosis and accompanying, intensive early education of at-risk children would lead to better results in school – because dyslexia is not a learning or intelligence deficit!

Special Background: Stroke (Apoplexy)

The term stroke, or apoplex, refers to a suddenly arising disease of the brain leading to continuous loss of function in the central nervous system and that is caused by the occlusion of a brain-supplying vessel (ischemia) or by a hemorrhage in the brain.

The stroke is caused by an undersupply of oxygen and nutrients to the brain cells. The consequent symptoms of such an event are, for example, impaired vision, disequilibrium, paralysis, headache and speech impairment. Symptoms vary in severity in association with the location of the event.

The time window for acute treatments available today is maximally 4.5 hours. The efficacy of treatment even within this window declines rapidly while the complication rate climbs. The somewhat difficult diagnosis as well as inadequate awareness in the public for the need for acute treatment lead to the result that less than 2 percent of the patients in Germany are successfully treated to the full extent possible. Therefore, 40 percent of patients pass away in the first year after the stroke and an additional 40 percent retain some level of disability requiring assistance. This makes stroke the third most common cause of death and the most frequent cause for disability in adults.

Special Background: Dyslexia

Dyslexia is a complex disorder that affects ca. 4 percent of all school children. It is characterized by difficulties in learning reading and/or writing. Affected individuals are challenged by problems transferring spoken language into written and vice versa. As dyslexia occurs more frequently within families, a genetic predisposition to the disorder is suspected; however, other causes are being discussed in parallel such as disorders of the auditory and visual cognition as well as language processing. While one finds assumptions of lowered intelligence in early descriptions of dyslexia, already in the 19th century, discussions are of innate "word-blindness" with normal intelligence. If dyslexia is recognized early, promoting "phonological awareness" can successfully treat it.

Cardiorepair Group

Products/Services
- induction of myocardial infarction and ischemia/reperfusion injury
- development and optimization of cell therapies in the field of cardiovascular diseases
- small and large animal models for myocardial infarction and ischemia/reperfusion for active agent and procedure testing
- cell culture models for active agent testing with heart muscle cells
- animal models for the development of drug delivery systems

Competencies
- small animal surgery
- functional and molecular analyses
- measurements of right and left heart function (ultra-miniature tip-catheter, echocardiography)
- cell labeling, immunohistochemistry
- analysis of gene and protein expression

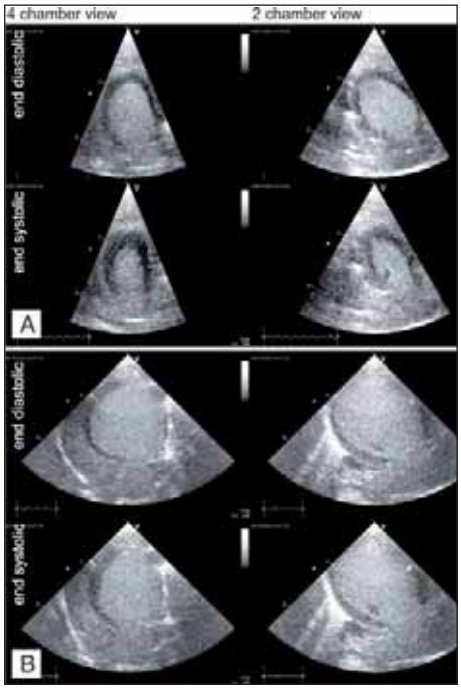
More services of the group can be found on pages 28-30.

Selected Project:
Cell Therapy and Cardio-protection During Myocardio Ischemia

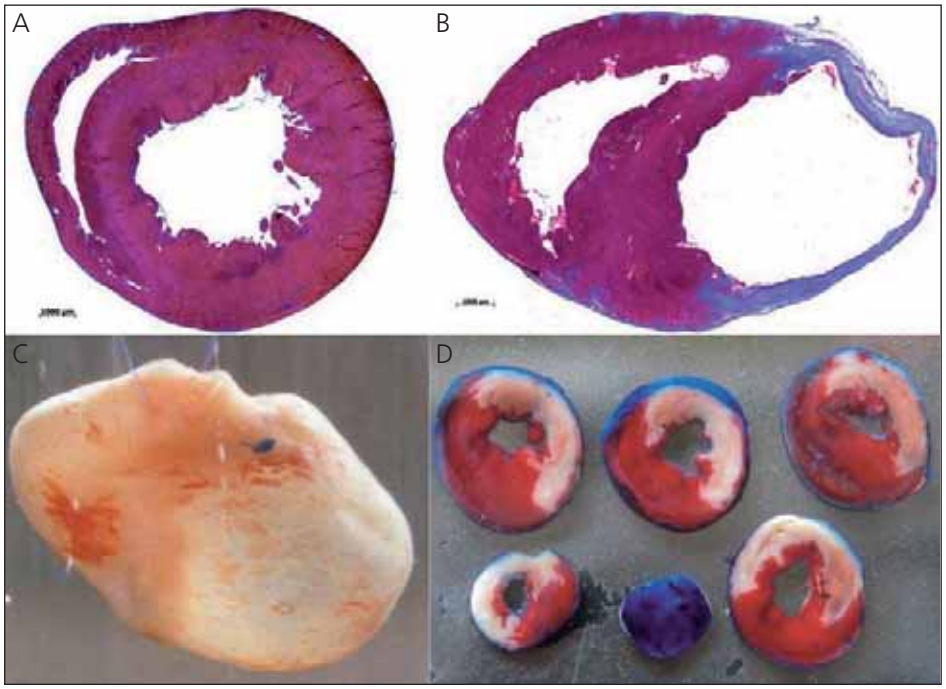
Background
Heart disease, particularly coronary heart disease and myocardial infarction is leading cause of death worldwide. Besides high mortality after acute coronary artery occlusion, the irreversible loss of cardiomyocytes and the resulting process of cardiac remodeling leads to progressively reduced cardiac pump function and ultimately heart

Contact
Dr. Alexander Deten
Phone: +49 (0) 341/355 36-3505
alexander.deten@izi.fraunhofer.de

This group aims to develop cell-based and cardioprotective therapeutic strategies for ischemic heart disease. The effectiveness regarding relevant functional parameters and the underlying mechanisms are studied in *in vivo* models of myocardial infarction, ischemia/reperfusion and ischemic preconditioning in small animals.



Echocardiographic measurement of heart function after contrast medium injection in apical 4-chamber (left) and 2-chamber view (right) 12 weeks after mock operation (upper panels) or myocardial infarction (lower panels) in rats.



Histological analysis of rat hearts (Masson´s trichrome; blue = collagenous infarct scar) 8 weeks after mock operation (A) or myocardial infarction (B) by permanent coronary artery occlusion. Mouse heart 4 weeks after coronary artery ligation (C). Visualization of injured myocardium of rat heart by TTC staining (white = ischemic area; red = vital myocardium) after ischemia for 60 minutes and subsequent reperfusion for 24 h (D).

failure. The acute mortality after myocardial infarction decreased in the past years due to improved early recognition and the timely start of therapy. However, there are only limited therapies available to effectively treat impaired heart function and developing heart failure.

Aims

The group aims to develop cell-based therapeutic strategies for ischemic heart disease in small animal models of myocardial infarction and ischemia/reperfusion injury. Furthermore, we are studying the underlying mechanisms in order to enhance and optimize the treatment process in order to improve cardiac pump function.

In further studies, cardioprotective mechanisms and ischemic preconditioning are investigated and strategies for an effective application of cardioprotective agents are tested. These studies aspire to provide protection to the cardiomyocytes from ischemic or stress-induced injury.

The entire experimental setup had to be designed in such a way that the application of any other cell product or cardioprotective agent, that may be, for example, provided by partners, could be tested and compared to the already developed protocol.

Results

The data indicate that the effects of cell therapy are predominantly mediated by paracrine mechanisms and cellular interactions. Furthermore, cell-specific factors as well as timing and route of application have a major impact on cell therapy efficacy. However, extensive cardiac regeneration was not observed after local or systemic application of different cell populations. Further studies aim to continually improve the treatment protocol and to specifically target the cardiac remodeling process after ischemic injury.

The investigation of cardioprotective mechanisms revealed that cytokine expression induced by ischemia as well as the resulting infarct size and cardiac function can be improved acutely after myocardial infarction. Further studies will show if such a treatment will have beneficial effects over a prolonged period of time.

Potential

The applied *in vivo* models of ischemic heart disease build the basis for further investigations of mechanisms and effectiveness of a variety of cell-based and cardioprotective therapeutic strategies to improve the currently limited treatment options of myocardial infarction and heart failure. Moreover, they can be utilized to analyze new drug delivery technologies and to test different diagnostic and therapeutic markers.

Vascular Biology Group

Products/Services

- identification of microbial expression profiles in tissue and bodily fluids
- testing the effect of defensins and antimicrobial peptides on the growth of bacteria
- evaluation of gene expression profiles in stress situations in endothelial cells and fibroblasts

Competencies

- microbiology of aerobic and anaerobic bacteria
- cultivation of cariogenic bacteria in biofilms under *in vitro* and *in vivo* conditions
- flow mechanics (rheology) and flow testing system
- technologies for the determination of genetic expression profiles

Bacteriocin:
antimicrobial peptide (AMP)

More services of the group can be found on pages 28-31.

Selected Project:
Development of a Therapy Against Cariogenic Bacteria

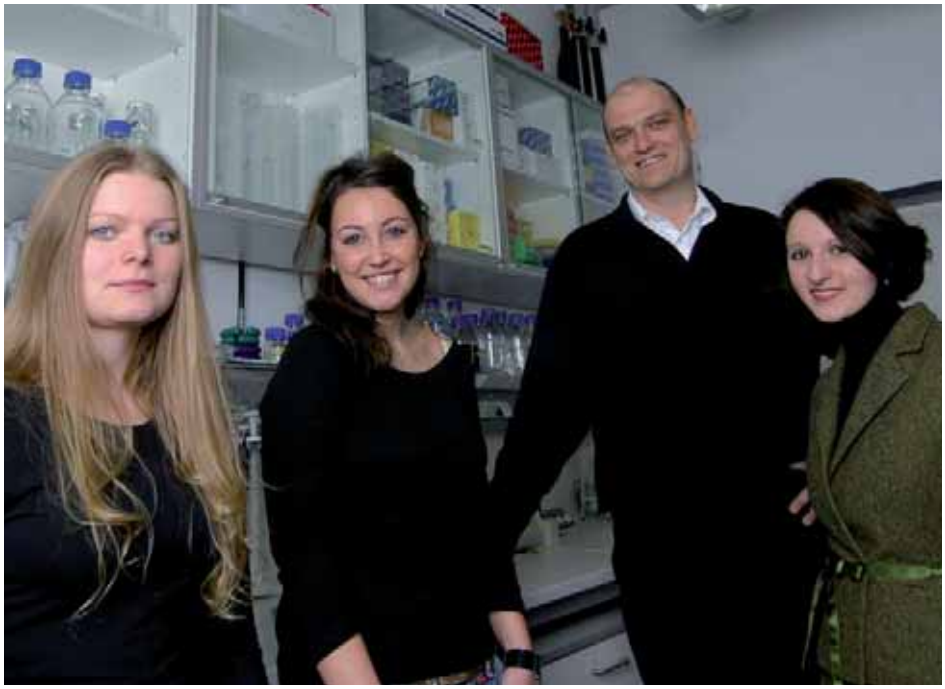
Background

Dental caries is the most widely spread and most expensive infectious disease in the western industrialized nations. Alone in Germany, over 10 million teeth are pulled each year due to dental decay or parodontitis. Although it is well known that a reduction in sugar consumption can significantly prevent caries, this fact is not reflected in the dietary consciousness of the public. With this in mind, the demand appears

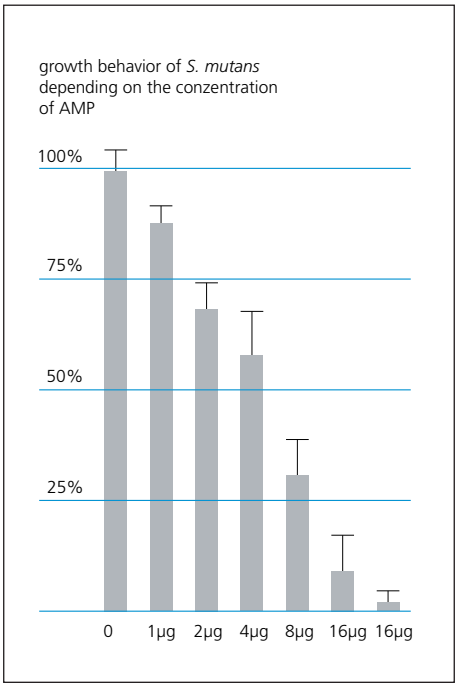
Contact

Dr. Andreas Schubert
Phone: +49 (0) 341/355 36-5105
andreas.schubert@izi.fraunhofer.de

The goal of this group is in the development of a preventative and at least partially curative gene therapy for artherosclerosis. Using vascular models, genes and promoters are identified that can be activated by biomechanical forces like flow or stretching. Because cardiovascular disease is often induced by dental disease (caries, parodontitis), a second focus of the group is on the establishment of a therapy against oral streptococcus.



Vascular Biology Group.



The effect of the antimicrobial peptide AMP-SM1 on the growth behavior of *Streptococcus mutans*.

pressing for the establishment of new therapies against the main germs causing caries *(Streptococcus mutans, Streptococcus sobrinus)* and similarly parodontitis *(Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis)*. Currently, the group is pursuing several alternative strategies in an effort to fight cariogenic and parodontopathogenic germs. In this endeavor, it has proven useful knowledge that bacterial competition for restricted sustenance in the biofilm of teeth is fierce. Therefore, certain bacteria species often secrete bacteriocins that are hardly immunogenic, but to some extent have a strong antibiotic effect.

Aims

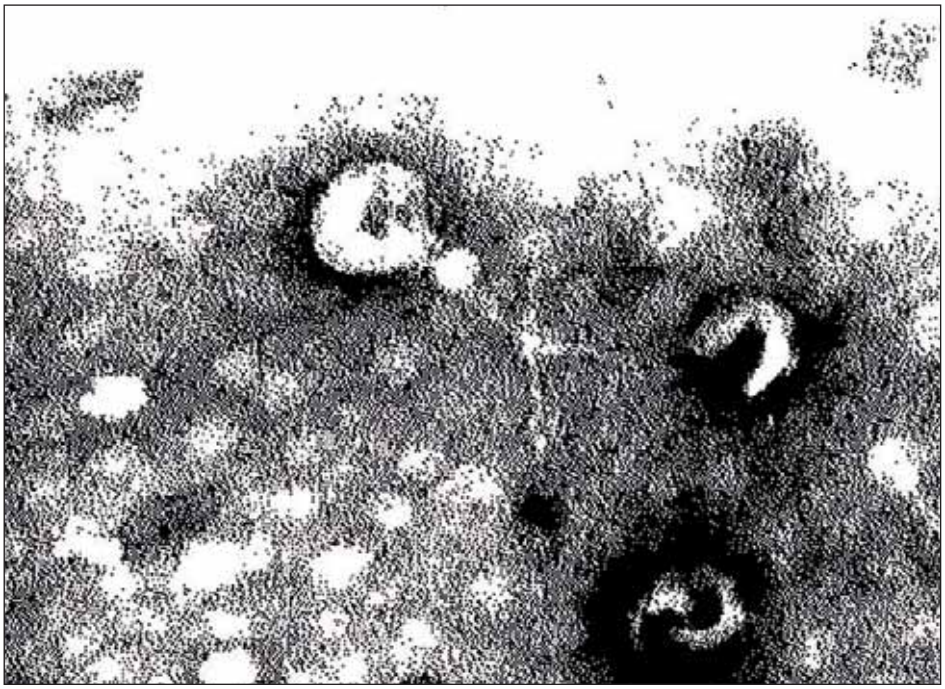
Our task was to identify the antimicrobial peptides (bacteriocins) that selectively inhibited cariogenic and parodontopathogenic germ growth or respectively mortified them. Based on known bacteriocins, sequences or sequence motifs were identified that had a bactericidal or at least a growth inhibiting effect on defined oral germs. Parallel to this, our cooperating partners at the University Hospital Homburg/Saar will produce, from patient samples, individual biofilm profiles via MALDI-TOF with regard to germ number and spectrum as well as aggressive behavior of defined bacteria based on the differential expression of surface proteins.

These combined efforts should allow an individualized treatment regimen for cariogenic and parodontopathogenic germs in the future.

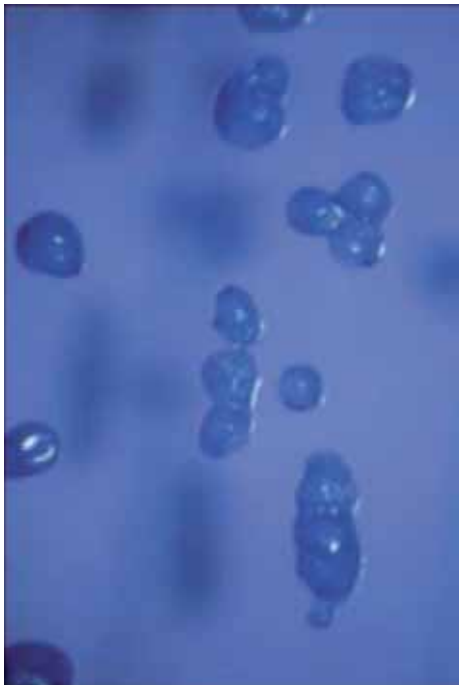
Results

48 antimicrobial peptides (AMP) have been tested for their effect on the growth behavior of *Streptococcus mutans, Streptococcus sobrinus* and *Lactobacillus spec.* The results are exemplarily depicted by the sample in the first graphic.

Multiple sequence motifs were identified that show a clear concentration and time-dependent growth inhibiting effect on specific bacteria species. However, it was also shown that affiliation to a particular bacteria type is not a sufficient criterion to determine sensitivity to a specific bactericide or antimicrobial peptide.



Electron microscopic image of a bacteriophage.



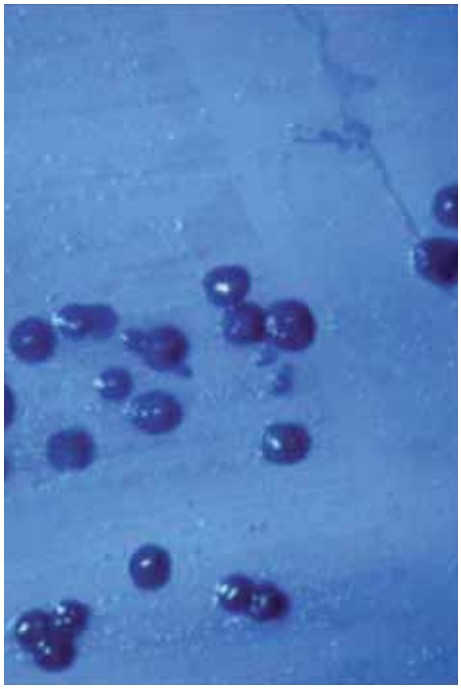
Bacteria colonies of *Streptococcus salivarius*.

It was also evident that the differing protein expression patterns of the bacteria (e. g. the expression of peptidases/proteases) were crucial to their sensitivity to a specific bacteriocin/AMP. In order to analyze the influence of a defined amino acid sequence of AMP on the growth behavior of the bacterium, the known sequence motifs were modified in key positions by similar amino acids.

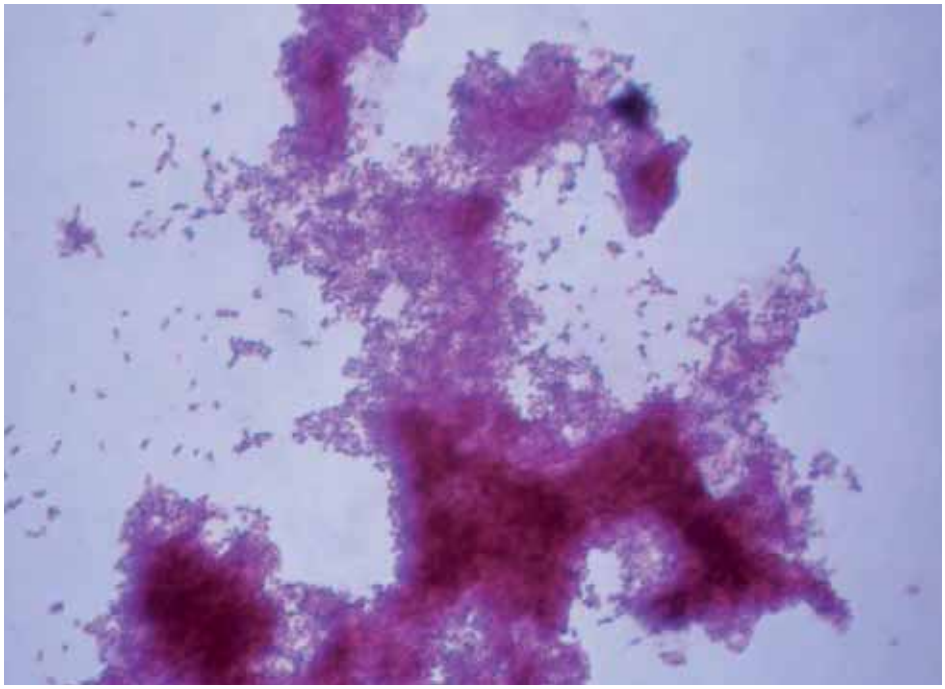
Potential

The first results are very promising, especially as they are in principle transferrable to other pathogenic germs. For this reason, the isolated bacteriocins are being collected into a sample bank as well as a databank. This will help make possible very extensive experiments, also high throughput assays, on other problem germs (MRSA, Salmonella, etc.).

Furthermore, lysogenic phages or enzymes could be isolated from cariogenic bacteria. Such phages would have the capacity to lyse cariogenic bacteria or, by reducing the biofilm, destroy their source of subsistence. All of these therapeutic strategies exhibit a high potential and will be tested *in vivo* soon. An essential advantage to our strategy is that AMP is very cost-effectively produced and that developing resistance against this new class of antibiotic would be significantly more difficult than to the antibiotics used today due to the structurally dependent multi-functionality of the peptides.



Bacteria colonies of *Streptococcus mutans*.



Mutan (Erythrosine B stained).

RNomics Group

Products/Services

- miRNA and ncRNA isolation from cell cultures, tissues, or blood; miRNA/ncRNA identification and quantification using microarrays, tiling arrays, quantitative RT-PCR, or ultra high throughput sequencing; development of miRNA and ncRNA biomarkers
- functional characterization of miRNAs and ncRNAs; overexpression and knock-down; identification of binding partners; development and testing of ncRNAs as drug target candidates
- analysis of transcriptome and UHTS (Solexa, 454, RNAsolid) data sets; annotation and classification of novel transcripts; prediction of RNA structures and interaction partners (targets)
- service provider for all types of array experiments based on Affymetrix technology; genome wide tiling array experiments, custom array design and implementation, custom ncRNA arrays
- genome-wide measurement of transcription factor binding sites and epigenetic properties, such as methylation state

Competencies

- microRNA and ncRNA transcriptomic
- molecular and cell biology of ncRNAs
- bioinformatics
- microarray technologies
- chromatin-immunoprecipitation-on-chip

More services of the group can be found on pages 30 und 31.

Selected Project: Analysis of Non-coding RNAs in Diseases

Background

Recent transcriptome projects have dramatically changed our view on how the genome is organized and regulated. The bulk of the genome is transcribed – but most of the transcripts are not translated into proteins. These non-protein coding RNAs (ncRNAs) emerge

Contact

Dr. Antje Kretzschmar
Phone: +49 (0) 341/355 36-5206
antje.kretzschmar@izi.fraunhofer.de

Dr. Jörg Hackermüller
Phone: +49 (0) 341/355 36-5205
joerg.hackermueller@izi.fraunhofer.de

The RNomics Group identifies and characterizes disease-associated non-protein coding RNAs (ncRNAs) for the development of novel diagnostic markers and therapeutic targets. The group develops experimental and bioinformatic methods for this task with a special focus on a general, disease- and system-independent applicability.

RNomics Group (left to right): Dr. Kristin Reiche, Katharina Schutt, Dr. Jörg Hackermüller, Kerstin Ullmann, Dr. Antje Kretzschmar, Prof. Dr. Peter Stadler, Prof. Dr. Friedemann Horn, Christine Schulz.

Microarrays allow the parallel detection of hundreds of expressed micro RNAs when searching, e. g. for tumor associated RNAs.

as an important layer of cellular regulation. However, the function and properties of ncRNAs are still poorly understood: We are facing a large number of novel, in most cases functionally uncharacterized ncRNA classes – and without much doubt, an enormous number is yet to be discovered.

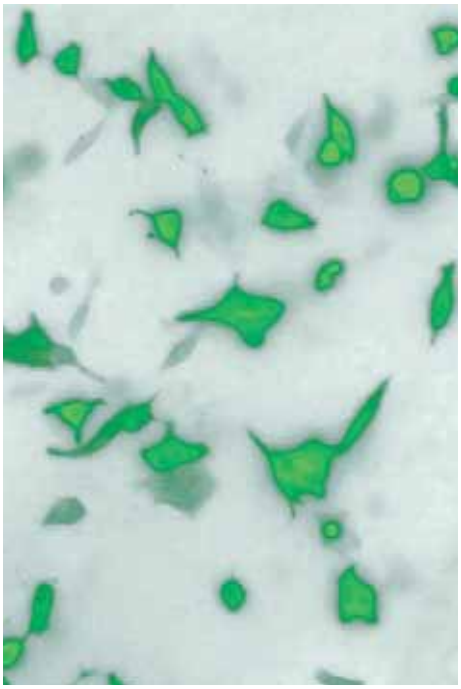
MicroRNAs (miRNAs) constitute the to date most thoroughly investigated class of ncRNAs. It has become obvious that they play a crucial role in the pathogenesis of a variety of diseases, such as cancer. But also for longer ncRNAs, an association to various disease or differentiation states has been shown. Consequently, the analysis of expression profiles of ncRNAs has a tremendous potential for the identification of diagnostic/prognostic markers and therapeutic targets. With the goal to introduce these novel transcripts into clinical applications, their identification, quantification and functional characterization has attracted much attention from clinical research and pharmaceutical industry.

Aims

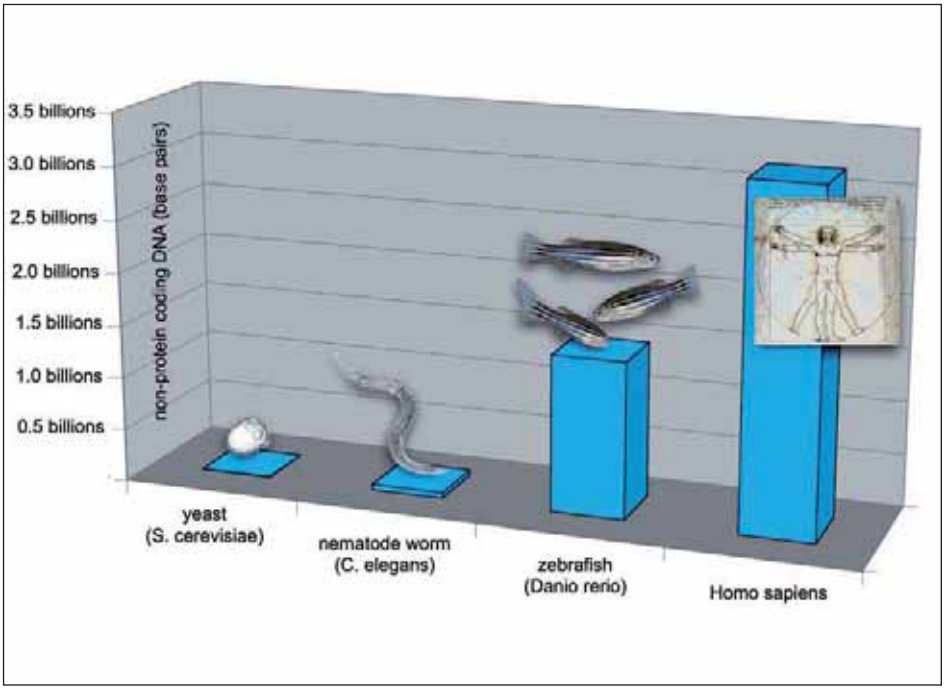
The ENCODE Project (ENCODE Project Consortium, Nature 2007), the RNomics Group has been participating in, has shown that virtually the whole genome is transcribed into RNA. This raises the question of the extent to which these transcripts are of functional importance for the cell – and in particular for diseased cellular stages. There is a need to investigate whether these newly identified ncRNAs are associated with diseases or disease stages, and if they play causal roles in the pathogenesis thereof. Another open question is the regulation of ncRNAs by hormones or signalling molecules that are important for a particular disease.

From a methodical point of view, the applicability of tiling arrays – proven by ENCODE to be of great value for the detection of transcription – to identify differentially expressed ncRNAs needs to be investigated.

An emerging alternative method to tiling arrays is ultra high throughput sequencing (UHTS) of transcriptomes. To analyze the data obtained by UHTS, novel methods and algorithms need to be developed, e. g. to efficiently map millions of short and in many cases inaccurate sequence fragments to a reference genome.



Prostate carcinoma cells appear to be less proliferative after overexpressing a particular ncRNA.



Genomic non-coding sequences increase with the complexity of organisms.

Results

In collaboration with Affymetrix Inc., the ENCODE transcriptomic approach has been extended to cover the entire genome and to include the detection of short RNAs (Kapranov, Science 2007). We have been able to demonstrate that a significant portion of long ncRNAs is used as a source for short transcripts and identified three novel classes of ncRNAs.

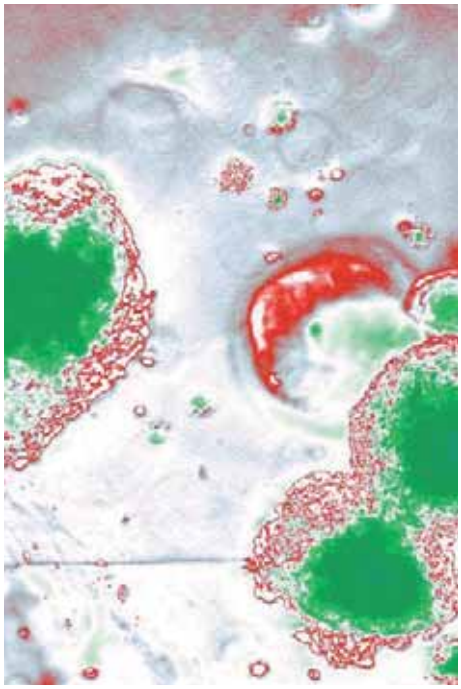
As a model system for the aberrant expression of ncRNAs in diseases and disease stages, ncRNA expression in prostate carcinoma cell lines was studied. Tiling array, miRNA microarray, and RT-PCR-based experiments led to the identification of differentially expressed miRNAs and ncRNAs that might provide a means to distinguish hormone-dependent from -independent prostate carcinoma types.

Together with researchers from the University of Leipzig, a miRNA capable of inhibiting the programmed cell death (apoptosis) of tumor cells, thereby contributing to tumor pathogenesis, has been investigated. Detailed analyses of the regulation of the miRNA allowed to link it to a signal pathway important for carcinogenesis (Löffler, Blood, 2007). To further characterize novel disease-associated ncRNAs, methods have been developed to efficiently inhibit these molecules.

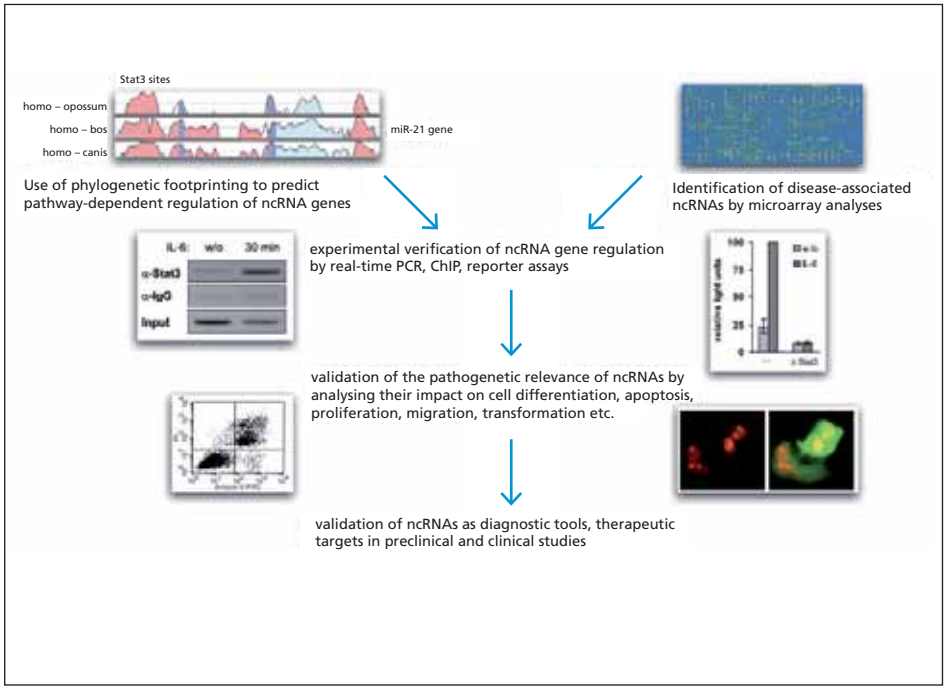
Potential

To evaluate their potential as biomarkers or therapeutic targets, differentially expressed ncRNAs in prostate carcinoma and other tumor models will be analyzed in primary tumor material to further evaluate their potential as biomarkers or therapeutic targets: We will particularly focus on ncRNAs regulated by disease-relevant signalling pathways. A genome-wide analysis of ncRNA expression regulated by a particular oncogenic pathway has already been conducted.

A large number of excellent reports on the disease association of ncRNAs and miRNAs increasingly raises the interest of academic as well as industrial research for this field. Therefore, developing and offering methods for the identification and quantification of non-coding transcripts will consequently find a growing market over the next few years. With a portfolio of established techniques, including microarray-, PCR, and UHTS based methods, the RNomics Group is excellently positioned for this task.



Agressive prostate carcinoma cells being evaluated for invasiveness.



Building a generic approach for the identification of disease associated ncRNAs from a combination of various wet-lab and bioinformatic techniques.

Growing knowledge of the disease association of ncRNAs will also raise the demand for functional analysis methods. Given the number of novel transcripts, this requires an appropriate automation of processes, which is a topic to which the RNomics Group will increasingly contribute.

Special Background

ncRNAs constitute the part of the cell's transcriptome that does not carry a signal for their translation into protein. Of the some 3.3 billion bases of the human genome, only about 1.5 percent code for proteins. Recent studies have found that the overwhelming, non-protein coding part of the genome is also transcribed with considerable activity into RNA. Expression of ncRNAs is regulated with high specificity and is associated with a remarkably large number of diseases.

This disease-relevance of ncRNAs represents a major field of research of the RNomics Group. Within international research consortia, however, the group also addresses basic questions, e. g. regarding the number and complexity of non-coding transcripts within the ENCODE consortium (ENCODE Project Consortium, Nature, 2007; Washietl, Genome Research, 2007), the relevance of small RNAs (Kapranov, Science 2007), structured ncRNAs in model organisms (Rose, BMC Genomics, 2008), or the bioinformatic annotation of novel ncRNAs (Athanasius F Bompfünewerer Consortium, Journal of Experimental Zoology, 2007).

Molecular Diagnostics Group

Products/Services

- identification of biomarkers
- testing active agents for immune modulating effects
- testing active agents for anti-inflammatory and destruction inhibiting activity (rheumatology)
- breath condensate analyses
- diagnostic gene profile analyses for clinical questions
- development and validation of laboratory diagnostic test procedures

Competencies

- automated mass spectrometry
- cell culture techniques
- flow cytometry
- cellular function tests
- multiplex measurements of cytokines and mediators
- automated microscopy

More services of the group can be found on pages 28-30.

Selected Project:
Genetic Markers for the Early and Differential Diagnosis of Rheumatoid Arthritis

Background

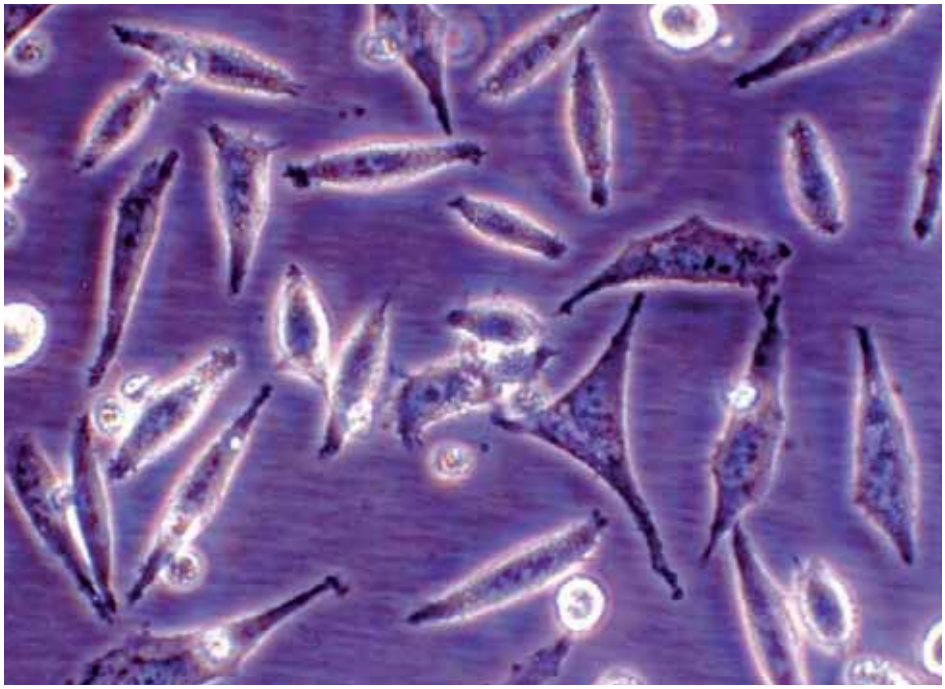
About 1-2 percent of the population in industrialized countries is affected by chronic rheumatic diseases, which in addition to causing pain and restricting mobility often incapacitate people for work and hence are a serious burden on society.

One problem with chronic autoimmune diseases, especially rheumatoid arthritis (RA), is that clear diagnosis is usually

Contact

Prof. Dr. Ulrich Sack
Phone: +49 (0) 341/97 25-506
ulrich.sack@izi.fraunhofer.de

The group is focused on the development of rapid, uncomplicated, immunologic, cell-based and genetic analyses and model systems for the field of transplant rejection, inflammation research and tumor biology – particularly for lung and joint diseases. In this way the group can implement innovative immunoassays, genetic analyses and complex cell culture models.



Invasive fibroblasts of patients with rheumatic arthropathies.

Dense cellular infiltration of inflamed joints.

only possible once the disease has already taken hold and inflicted serious harm on the body.

The therapies currently available cannot cure RA. In the event of very early diagnosis, however, the disease may potentially be cured. Initially, uncertain signs of RA occur in many people, but only about 20 percent actually develop chronic RA. Since the therapies used exert considerable side effects on the immune system and are very expensive, treating all cases of suspected RA is not an option.

Therefore, the possibility of using biomarkers for very early, reliable differential diagnosis is of high clinical relevance. Moreover, patients respond differently to different types of therapy. Although genetic variants and autoantibodies already known can make an important contribution, they are not sufficient for early, effective and individualized therapy of RA.

Aims

To make more efficient diagnoses, what needs to be done is to identify new biomarkers which either alone or in conjunction with known biomarkers will enable very early, clear-cut, individualized diagnosis so that the most suitable type of therapy can be decided. This is being carried out in association studies with markers that are disease-specific and individual-specific.

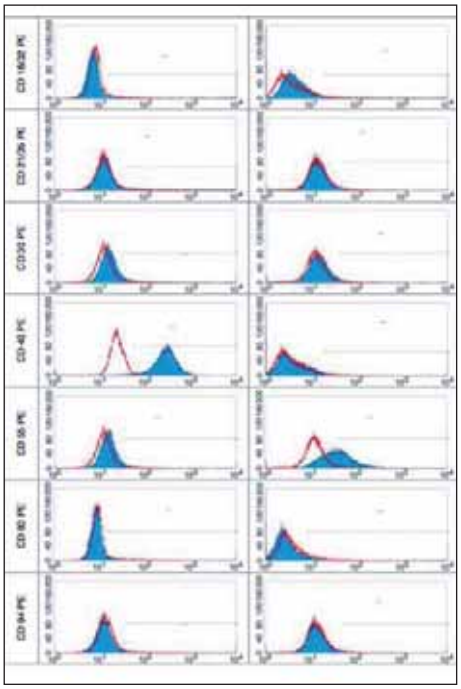
Biomarkers found to be important must then be verified and validated for clinical use. Other key issues include the use and further development of modern technologies for the identification of new biomarkers and their efficient, rapid and flexible development for diagnostic use.

Results

Mass spectrometry has been established and honed in the Molecular Diagnostics Group as a flexible, powerful platform technology for measuring genetic variants, quantitative gene expression and peptide patterns.

It is used for extensive genotype-phenotype association studies for RA and has enabled new markers to be identified. However, since they are not sufficient by themselves for the diagnostic applications envisaged, these markers are currently combined with known genetic markers, autoantibodies and peptides. Moreover, the use of automated mass spectrometry has also been prepared for the determination of known, clinically relevant genetic variants.

Optimal technical instrumentation allows for rapid screenings.



Flow cytometric comparison of invasive cells.

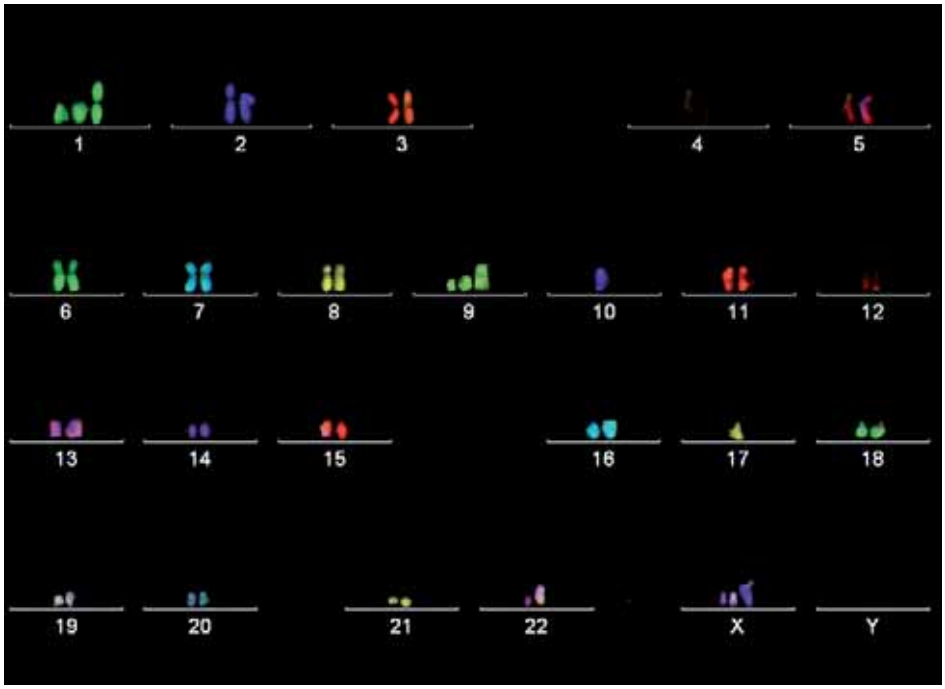
Potential

Given the group's expertise in designing and performing studies to identify biomarkers, similar studies can be offered for diverse questions – especially projects to identify disease-relevant genetic variants and pharmacogenomics for individualized therapy and the identification of new drug targets.

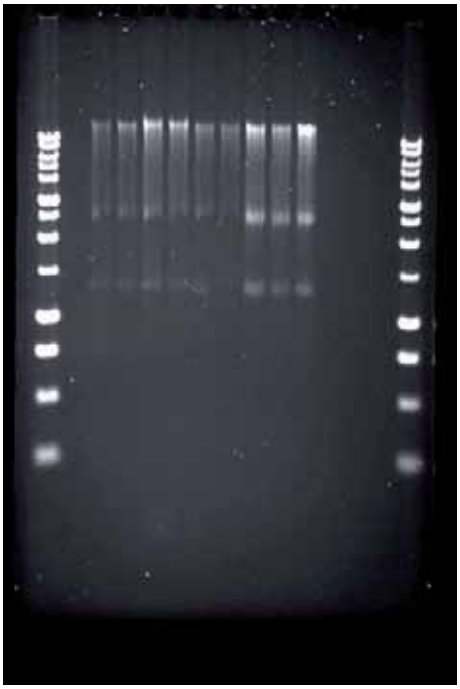
Such studies can also include the identification of peptide markers on the basis of automated MALDI-TOF mass spectrometry. Peptide markers identified from tissues enable mass spectrometry imaging in order to, for example, identify tumor cells in tissue sections.

Special Background: Individualized Medicine

Every person reacts individually to environmental influences, pathogens or noxa due to her or his unique genetic endowment. Moreover, as a result of this unique endowment medicaments have differing efficacies and side effects for each person. The specific diagnostic possibilities from our institute and the option to offer and develop individualized therapies provide the optimal conditions for the development and implementation of these types of medical procedures.

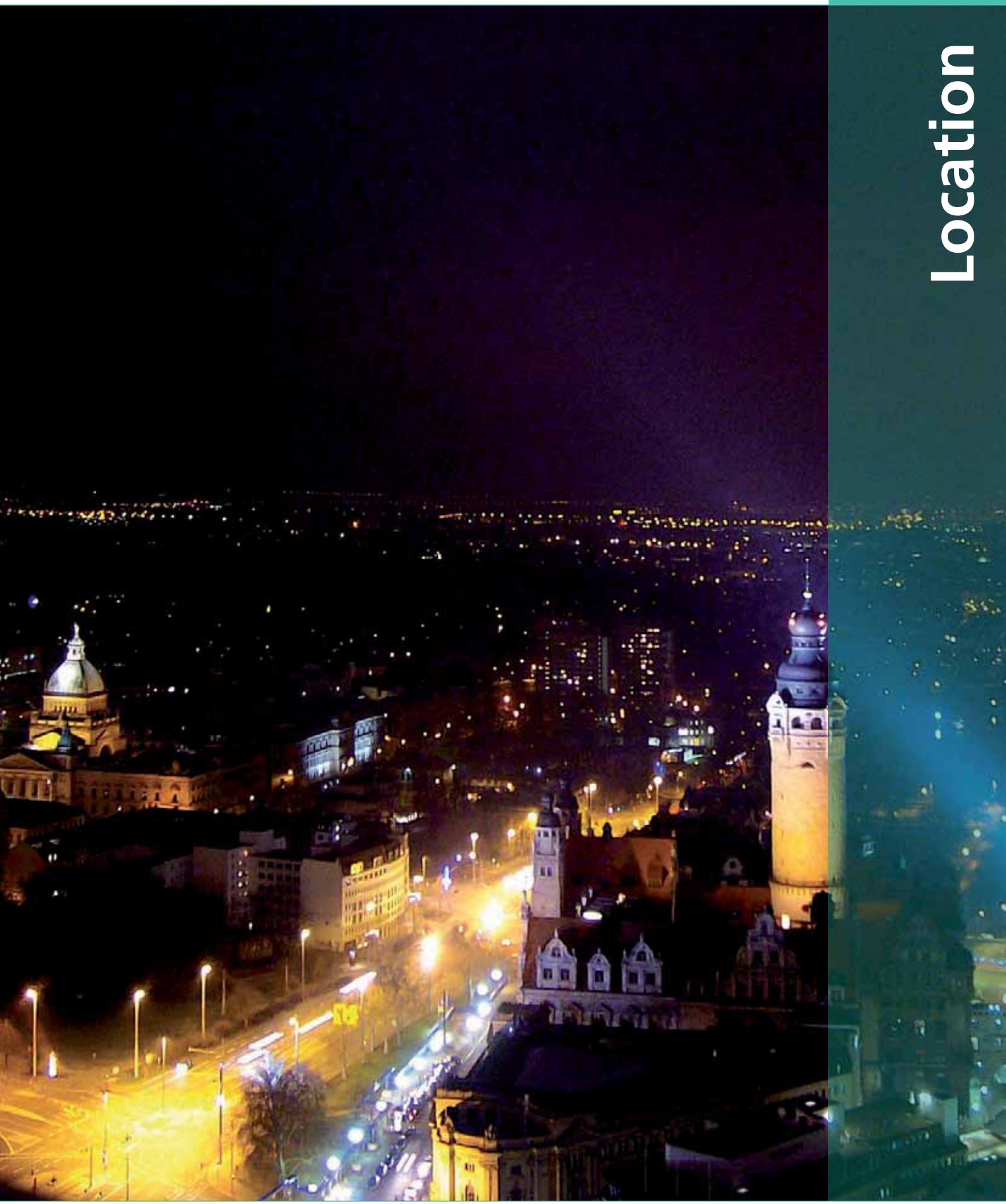


M-FISH analysis on metaphase chromosomes of a neuroblastom to detect genetic defects.



Quality control of mRNA via gel electrophoresis.

Location



BIO CITY

Funds from the Free State of Saxony and the city of Leipzig established the BIO CITY on the edge of the former convention center grounds in the southeast of Leipzig. This building complex cost 100 million euros, sits on 20,000 square meters and houses the Center for Biotechnology and Biomedicine of the University of Leipzig as well as industrial occupants; with more than 25 companies, the real estate is nearly fully occupied. Included in these companies are many cell technology enterprises like VITA34, International AG, Haemabank AG, Curacyte AG and NeuroProgen GmbH. The building is directly across from the German National Library at the Deutsche Platz, next to the Max Planck Institute for Evolutionary Anthropology and near the institutes and clinics of the Faculty of Veterinary Medicine of the University of Leipzig. The Faculties of Medicine, Chemistry, Physics and Biology, Pharmacy and Psychology are only minutes away from the building complex of the BIO CITY. The grounds are very accessible both by public transport (tram, bus or regional train) or by car and only ten minutes from the city center. Ninety-nine percent of the spaces in BIO CITY are rented. Many companies are attracted to the location due to its bringing together of university and industry-near research with innovative enterprises under one roof. For this reason, it is planned that the BIO CITY will extend its commercial portion in 2008-2010. This third construction period will be financed by the Free State of Saxony and the "Leipziger Gewerbehofsgesellschaft" (LGH). The new building will provide over 5,500 square meters of additional real estate for companies already present in the complex and for new occupants or spin-offs.

Foyer of the BIO CITY.

View on the new building, status april 2007.

In this interesting scientific and entrepreneurial context, the Fraunhofer IZI has established its initial organization by renting one of the wings of the BIO CITY. Our staff make use of the conference rooms and cafeteria as well as the events organized by Bionet GmbH, which is responsible for the marketing of the BIO CITY and extending Leipzig's reputation as a significant location for health research.

The New Fraunhofer IZI Building

The accommodation in the BIO CITY is, however, only a stopover until the new building for the institute is completed. It is currently under construction and becoming visible as a new neighbor to the BIO CITY; in spring 2008, we will occupy it.

The new home of the institute will comprise over 1600 square meters of laboratory and 1600 square meters of office space as well as provide over 450 square meters for GMP laboratories. The building will provide space for a total of 200 staff. The real estate was made available by the city of Leipzig on a long-term, no-cost lease. After the foundation stone ceremony in September 2006, construction continued as planned in 2007. The building shell and technical fitting will be completed by the end of the year.

From left to right: Martin Schmirander (architect), Frank Richter (statics) und Michael Weese (construction department of the Fraunhofer-Gesellschaft).

Topping Out Ceremony for the New Fraunhofer IZI Building

On the afternoon of May 31, 2007, more than 150 guests gathered in the atrium of the new building to celebrate the traditional Topping Out Ceremony. Mr. Michael Weese from the construction department of the Fraunhofer Central Headquarters in Munich summarized the construction plan, described the phases, the genesis and furthermore wished, "an accident and disturbance-free course." Then the director of the institute, Prof. Frank Emmrich welcomed the guests – particularly the planners and the builders – to "their ceremony." He reported about the many curious looks directed at the new feature on the landscape and the webcam that is focused on it from the neighboring BIO CITY. The staff of Fraunhofer IZI is looking forward to the new laboratories and the state-of-the-art equipment. Martin Schmirander of Heinle, Wischer & Partners spoke for the architects about the building and compared the cell-like comb of the façade to the content of the institute. He noted the adherence to the planned deadlines, so that nothing more should stand in the way of the planned occupation of the building in spring 2008.

After the greetings and welcome, the traditional proclamation and topping out ceremony speech were given by the construction leader, Kay Alert. Representatives of the principals and of the architecture and statics offices drove in the last nail with bravura. Then, Professor Emmrich opened the rich buffet and thus the evening rang out with pleasant company, cool beer and fresh suckling pig.

1 Translational Centre for Regenerative Medicine (TRM)

In 2006, the Translational Centre for Regenerative Medicine was founded in Leipzig and installed in immediate proximity to the BIO CITY and Fraunhofer IZI. The TRM is a part of the excellence grants from the federal ministry of education and research and the Free State of Saxony. Institutes from across five faculties are integrated into the TRM, which is directed by Prof. Emmrich, to build four Research Areas: Tissue Engineering and Materials Science (TEMAT), Cell Therapies for Repair and Replacement (CELLT), Regulatory Molecules and Delivery Systems (REMOD) and Imaging, Modelling, and Monitoring of Regeneration (IMONIT). Conceptional, preclinical and clinical research projects are supported by the TRM. The initial grant for the institution is 20 million euros over four years. The Free State of Saxony is providing an additional 17 million euros for building renovations and basic equipment. As well as playing a key role in the application to establish TRM, Fraunhofer IZI also maintains diverse links with the TRM.

2 Interdisciplinary Centre for Clinical Research (IZKF)

The Interdisciplinary Centre for Clinical Research Leipzig was founded in 1996 as a center of excellence of the federal ministry of education and research at the Faculty of Medicine to initially focus on cell-cell and cell-matrix interactions of diagnostic and therapeutic significance. Scientific focuses are on immunology, endocrinology, neurosciences and oncology. The centre also maintains various junior groups and the service units specializing in DNA sequencing and peptide technology.

3 Center for Biotechnology and Biomedicine (BBZ)

In the framework of the Biotechnology Initiative of the Free State of Saxony, five faculties joined together to create a key project to be established in the BIO CITY Leipzig: thus the Center for Biotechnology and Biomedicine was founded. The Free State of Saxony granted 200 million euros to establish the BIO CITY, including the BBZ. Particular support for Fraunhofer IZI is expected from the BBZ Members in the areas of Cell Techniques and Applied Stem Cell Biology, Bio-process Technology, Protein Structure Analysis, Mass Spectroscopy, Molecular Cell Therapy and Molecular Pathogenesis.

Clinical Competence

Leipzig's clinical profile is characterized by particular expertise in the fields of cell and tissue transplantation. For example, heart and lung transplants are carried out at the Heart Centre Leipzig, while the University Hospital specializes in liver, kidney and pancreas transplants. In addition, the José Carreras Foundation has opened a bone marrow transplant center, while the German Organ Donation Foundation (DSO) has set up a logistics center for tissue conservation.

4 University Hospital

The University Hospital is associated with one of the oldest medical training locations in Germany. Research focuses of the hospital include neurodegenerative diseases like Alzheimer's disease, Parkinson's and retinal degeneration, immunological questions on immune reactivity, immunological tolerance as well as projects in molecular oncology.

5 Heart Centre

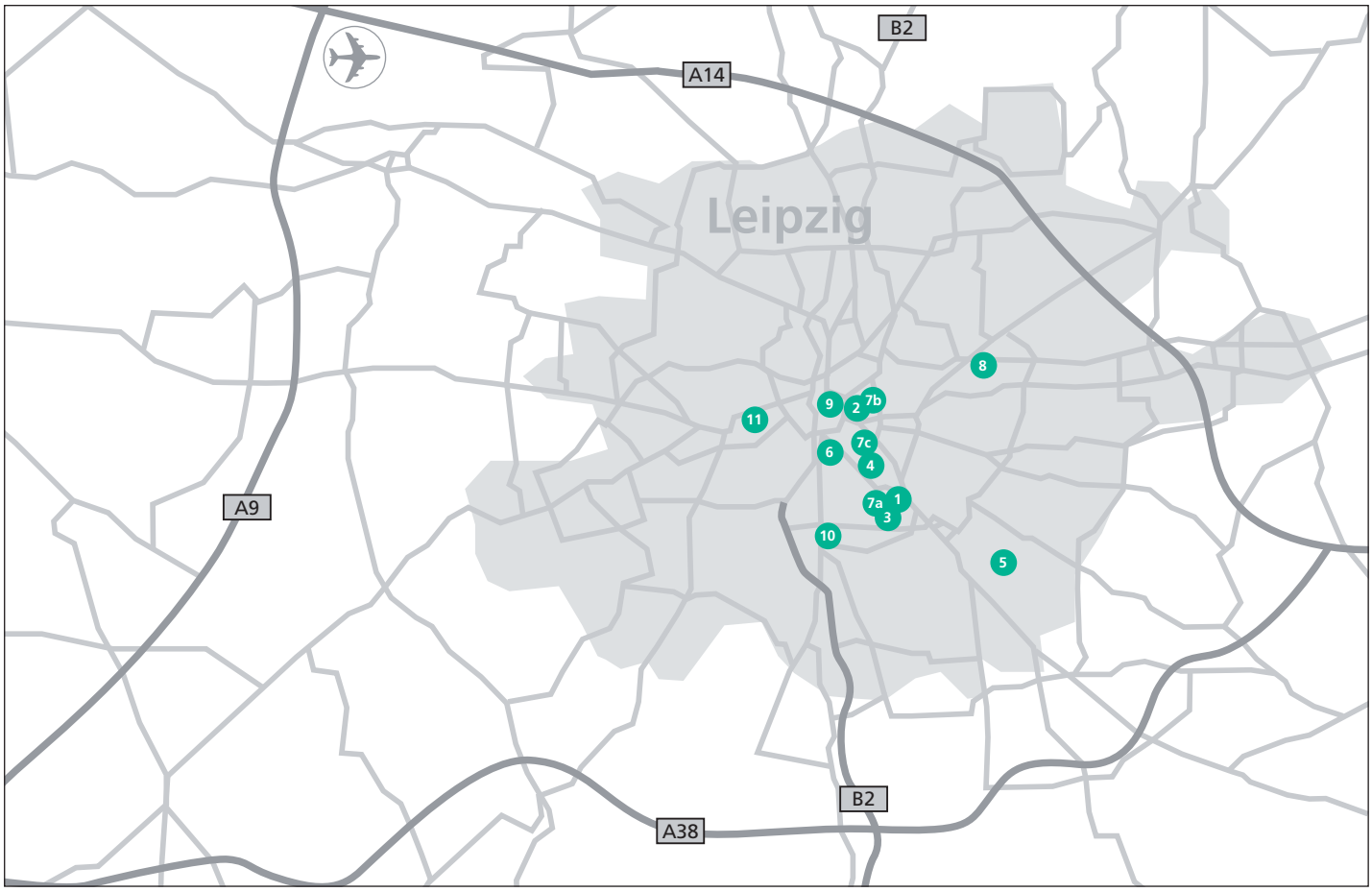
The Heart Centre Leipzig GmbH – University Hospital is a specialty hospital that houses cardiac surgery, internal medicine, cardiology, pediatrics and child cardiology. With 330 beds and 10 day-clinic places, the Heart Centre provides top-notch medical treatment for all aspects of the heart. Besides the clinical resources, research is a major activity at the Heart Centre, in particular in the areas of developing new operative techniques and cardiovascular basic research.

6 Coordination Center for Clinical Trials (KKSL)

Innovative structures for clinical research (i. e. planning and performing clinical trials) have become very successfully established in Leipzig. The federal ministry of education and research provided funding for the Coordination Center for Clinical Trials Leipzig (KKSL) where trial assistants and doctors can be trained and clinical studies devised. In addition, Innomed Leipzig GmbH's Center for Therapy Studies (ZET) is an organization that carries out clinical trials with doctors treating outpatients. Both institutions already work very closely with Fraunhofer IZI.

6 Interdisciplinary Center for Bioinformatics (IZBI)

Thanks to financial support from the German Research Foundation (DFG), Leipzig has established an Interdisciplinary Center for Bioinformatics (IZBI). Its main tasks are the modelling of mechanisms of cellular signal transduction and data processing for cell analysis techniques. In particular, Fraunhofer IZI's RNomics Group cooperates intensively with IZBI.



Translational Centre for Regenerative Medicine (1), Interdisciplinary Centre for Clinical Research (2), Fraunhofer Institute for Cell Therapy and Immunology (3), Center for Biotechnology and Biomedicine (3), University Hospital (4), Heart Center (5), Coordination Center for Clinical Trials (6), Interdisciplinary Center for Bioinformatics (6), Interdisciplinary Transgenesis Center (3), Max Planck Institute for Evolutionary Anthropology (7a), Max Planck Institute for Mathematics in the Sciences (7b), Max Planck Institute for Human Cognitive and Brain Sciences (7c), Center for Environmental Research (8), Leibniz Institute of Surface Modification (8), Association for the Advancement of the Health Economics of the Region Leipzig (3), University of Leipzig (9), University of Applied Science (10), Graduate School of Management (11).

3 Interdisciplinary Transgenesis Center

The Faculty of Veterinary Medicine, Faculty of Medicine and the Max Planck Institute for Evolutionary Anthropology joined forces to found a transgenesis center where pioneering techniques for the introduction and elimination of genes can be developed – for instance in connection with the development of new pathogenetic models in animals.

7a 7b 7c Max Planck Institutes (MPIs)

Cooperation with the three Max Planck Institutes in Leipzig is only natural. The Max Planck Institute for Human Congnitive and Brain Sciences (7c) provides special expertise for modern imaging technologies and very valuable facilities are accessible, like, for example, MRI. The MPI for Mathematics in the Sciences (7b) is the sponsor of the IZBI, besides the university. The cooperation between the MPI for Evolutionary Anthropology (MPI-EVA) (7a) (Prof. S. Pääbo) is especially interesting and has yielded internationally recognized research in molecular and developmental biology. Until the new Fraunhofer IZI building is completed, it is planned to house the RNomics Group at the MPI-EVA.

8 Centre for Environmental Research (UFZ)

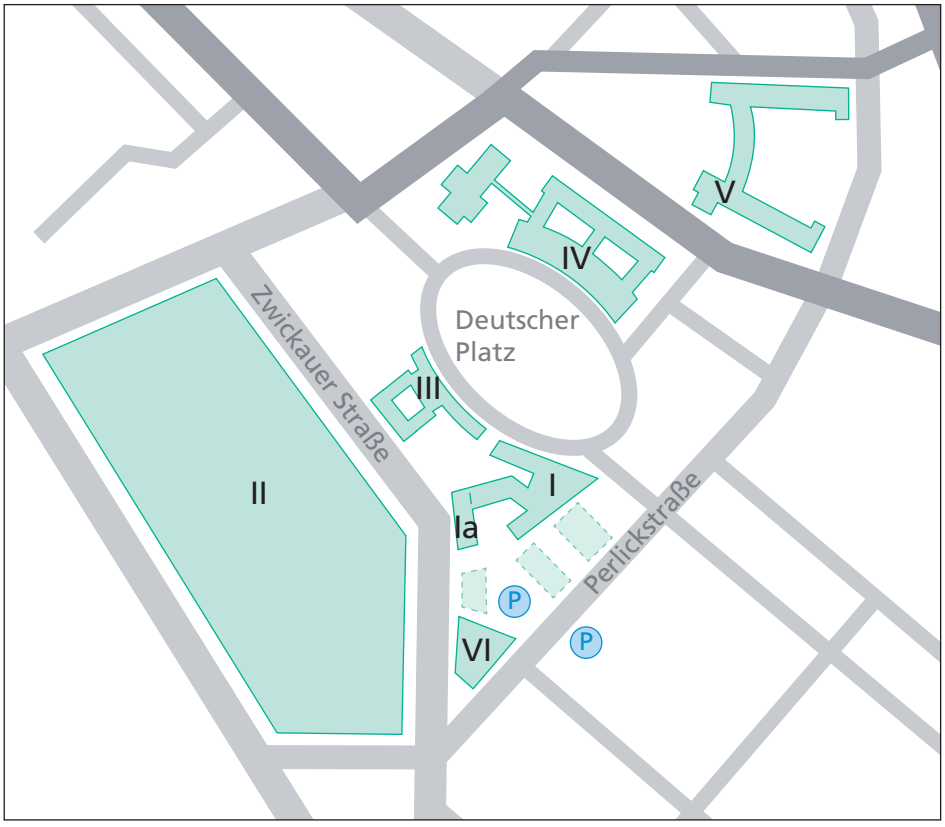
The Centre for Environmental Research (UFZ) Leipzig-Halle is a member of the Helmholtz-Gesellschaft and one of the German government's biggest research institutions. Many working groups there represent great technological experience with bioreactors for microbiolgy, sensor technology and cell breeding.

8 Leibniz Institute for Surface Modification (IOM)

The IOM carries out application oriented basic research with the goal of transferring their results into new technologies. Their focus is on examining the interactions between radiation and materials. Knowledge of physical and chemical processes support the development and production of insulating, metallic, semiconducting and polymer surfaces.

3 Association for the Advancement of the Health Economics of the Region Leipzig (VGF)

This association, founded in 2004, has the mission to promote the region of Leipzig as a leading center for medical science and practice in Germany and internationally. The group is composed of researchers, doctors, clinics, practices, laboratories and commercial partners. Contacts in the VGF are primarily scientists, industry members, interest groups, doctors, patients and the interested public.



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), new building of Fraunhofer IZI (VI).

Educational Environment

Renowned higher education institutions like the University of Leipzig, the Leipzig University of Applied Sciences (HTWK) and the private Graduate School of Management (HHL), which was re-founded after the unification of Germany, have a significant impact on the region's workforce. They are the basis for the high level of education and training one finds in the population: 14 percent are engineers or technicians and 16 percent hold a higher degree. This sets a great stage to recruit a well-trained staff.

9 University of Leipzig

The University of Leipzig was founded in 1409 and is one of the most steeped-in-tradition academic research institutions in Germany. Over 30,000 students are matriculated in Leipzig. In 2009, the university will celebrate its 600th anniversary with the opening of a massive new building complex that contains an Auditorium Maximum in the city center. The University of Leipzig has a strong partner in the Fraunhofer IZI for research cooperations as well as the expansion of our common teaching and professional development offerings. These contribute to raising the attractivity of the city. Also of particular interest is the connection to veterinary medicine as there are only five faculties for this field in Germany. For the mostly biological or medical research topics of Fraunhofer IZI, the direct contact to veterinary medicine with its many analogies to human medicine is a meaningful advantage for future developments.

10 Leipzig University of Applied Sciences (HTWK)

The Leipizg University of Applied Sciences dates back to 1764. As the largest institution of its kind in Saxony, it currently has more than 6000 students on 30 courses in the fields of engineering, economics, media and information science, computer science, mathematics and science.

11 Graduate School of Management (HHL)

The private Graduate School of Management (HHL) has proven to be an outstanding cooperation partner. A number of projects have been conducted in which medics and scientists have teamed up with business management students and junior lecturers to compile business plans and marketing strategies.

Cooperation

Research Partners

Federal Research Institute of Nutrition and Food, Kiel

Center for Cancer Research, MD, USA

Central Institute for Experimental Animals, Kawasaki, Japan

Charité Berlin, Institute for Fluid Mechanics

Charité Campus Benjamin Franklin, Berlin

University of Applied Sciences Lausitz, Senftenberg

HIV Drug Resistance Program, MD, USA

Leipzig University of Applied Sciences (HTWK), Leipzig

Institut Cochin, Paris, Frankreich

Max Planck Institute for Evolutionary Anthropology, Leipzig

Max Planck Institute for Infection Biology, Berlin

Hanover Medical School

National Institute for Medical Research, London, UK

National Institutes of Health, MD, USA

Oxford University, UK

Partner Institute for Computational Biology, Shanghai, China

The STEPS consortium, USA

University of Buenos Aires, Institute for Pathology, Argentina

University of Dresden, Department of Neuropathology

University of Essen, Institute for Pathology

University of Frankfurt/Main

University of Halle-Wittenberg

University of Hamburg

University of Hohenheim

University of Cologne

University of Leipzig

University of Leipzig, Centre of Biotechnology and Biomedicine (BBZ)

University of Leipzig, Carl Ludwig Institute of Physiology

University of Leipzig, Large Animal Clinic for Surgery

University of Leipzig, Heart Centre

University of Leipzig, Institute of Biology II

University of Leipzig, Institute of Medical Informatics, Statistics and Epidemiology (IMISE)

University of Leipzig, Institute of Virology

University of Leipzig, Institute of Medical Microbiology and Epidemiology of Infection

University of Leipzig, Hospital for Neurology

University of Leipzig, Hospital for Nuclear Medicine

University of Leipzig, Hospital for Radiation Therapy and Radiooncology

University of Leipzig, Hospital for Urology

University of Leipzig, Medical-Experimental Centre

University of Leipzig, Paul Flechsig Institute of Brain Research

University of Leipzig, Translational Centre for Regenerative Medicine

University of Leipzig, Faculty of Veterinary Medicine, Institute of Anatomy, Histology and Embryology

University of Leipzig, Faculty of Veterinary Medicine, Institute of Pathology

University of Leipzig, Centre for Radiology

University of Munich

Universitat Pompeu Fabra, Instituto Municipal de Investigación Médica (IMIM), Barcelona, Spain

University of Rostock, Hospital for Heart Surgery

University of Turin, Italy

University of Wien, Austria

University of Würzburg

University of Zurich, Institute for Veterinary Physiology, Switzerland

University Hospital Leipzig, Institute for Clinical Immunology and Transfusion Medicine

University Dental Hospital, Homburg/Saar

University Dental Hospital, Leipzig

University Nijmegen, Netherlands

University of Calgary, Canada

University of Michigan, USA

University of Queensland, Australia

University of Sevilla, Spain

University of Sheffield, UK

Universtitat Pompeu Fabra, Barcelona, Spain

Weizmann Institute of Science, Rehovot, Israel

Yale University, New Haven, USA

Research Cooperation

Antibody-Chimeras

The rejection of transplanted organs is one of the biggest problems in transplantation medicine. One branch of regenerative medicine focuses on measures that partially prevent life-threatening reactions of the immune system.

With this project, Fraunhofer IZI, ANTITOPE, an English company, and the University of Leipzig aim to develop a tolerance-inducing antibody to treat Graft-verus-Host-Disease. With this goal, a murine antibody has already been developed that has achieved promising results in model. The next step is to develop a chimeric antibody whose constant regions are of human and variable regions are of murine origin. Furthermore, a production cell line is being developed, for a large-volume production of the immunologically optimized antibody.

Ethiopia

Between 30 and 36 million people worldwide are living with HIV (2007 AIDS Epidemic Update, UNAIDS and WHO). The largest portion of infected individuals (ca. 70 percent) live in sub-saharan Africa. In Ethiopia alone, up to 3.5 percent of the population is infected with HIV. The co-infection rate of HIV with other pathogens (Plasmodium, Hepatitis C Virus, Leishmania, etc.) is unclear in Ethiopia. The development of resistances against antiretroviral medicaments also is not yet studied.

Fraunhofer IZI, in cooperation with local Ethiopian university partners, is building a reference bank in various regions of Ethiopia to advance the study of locally present resistances as well as co-infections. The Virus-Host-Interaction Group coordinates the project that examines the blood samples, which are collected in Ethiopia by our partner, Prof. Dr. Dieter Reißig, for HIV-subtypes and resistance development. In a field study by the Molecular Diagnostic Group, the correlation to T-cell number is being examined. The goal of the project in cooperation with the treating doctors is to adapt and thereby improve the care of patients in the region.

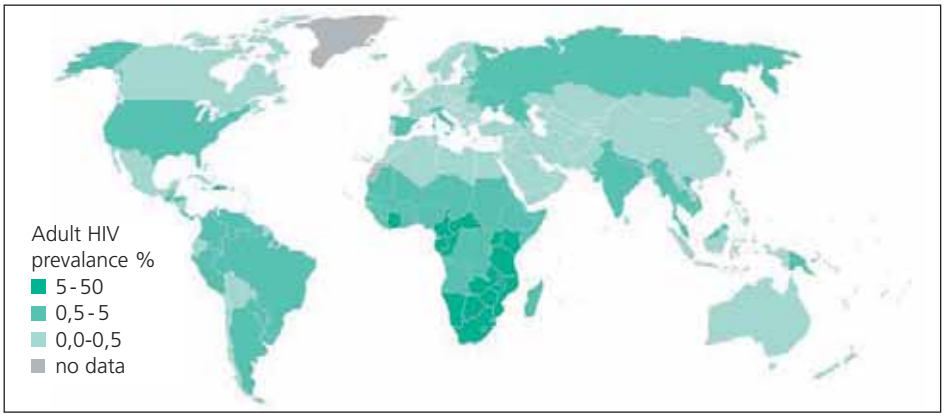
ENCODE

It is a fact that of the 3.3 billion base pairs of human DNA only about 1.5 percent code for proteins and therefore contribute to the basic construction of all human cells. The rest of the genome – approximately 3.25 billion base pairs – has been viewed up until now as genetic rubbish without any function worth mentioning.

In September 2003, the US American National Human Genome Institute founded a consortium with the goal of identifying all functional elements of the human genome sequence. The so-called ENCODE (**ENC**yclopedia **O**f **D**NA **E**lements) consortium is comprised of many international working groups and it includes Fraunhofer IZI's RNomics Group together with the University of Leipzig as the only German partner.

The international ENCODE research team succeeded recently in discovering that the segments of the genome that are termed "genetic rubbish" or non-coding genes are nearly entirely transcripted into RNA. Furthermore, these ncRNAs regulate the genes whose plan stipulates how proteins are constructed. If these processes malfunction, an imbalance in the cells can arise that may result in disease. These results present many new possibilities for diagnostics and will very surely be of therapeutic interest, for example, for cancer or heart attacks.

In June 2007, these promising results were published in the journal, Nature. In addition, the Fraunhofer IZI RNomics Group participated in a press conference in Leipzig about their work as a partner in ENCODE.



International comparison: percentage of HIV-infected persons and AIDS patients of the population, 2005. Data source: UNAIDS.

Large Scale Projects

ETOX-RAB – Alternative Methods to Animal Experiments

Deformities and birth defects are often caused by environmental influences, like the consumption of medicaments during pregnancy, in addition to genetic mutations. Most notably, substances that damage bone lead to congenital anomalies and skeletal deformations in fetuses during pregnancy. Such substances are termed embryo- or osteotoxic.

The project ETOX-RAB aims to determine the osteotoxic potential of new active agent candidates in early phases of drug development (preclinical), in order to exclude for relevant side effects. Currently, only animal experiments are available for such osteotoxic tests. The goal of ETOX-RAB is to reduce the number of these animal experiments. The new process allows testing *in vitro*, not in an animal. With the Embryonal Stem Cell Test (EST), the inhibitive effect of an active agent on the differentiation of murine embryonal stem cells is examined. Because of their pluripotent potential, embryonal stem cells can differentiate into all three germ layers of somatic cells and are therefore a suitable model for embryology. This project, which is funded by the federal ministry for education and research, is being carried out at Fraunhofer IZI in cooperation with partners from industry, technology development and different universities.

"Zellwerk"

The paradigm change from symptomatic treatment of degenerative diseases to causal eradication through organic implants with the help of tissue engineering is one of the most forward-looking research fields of regenerative medicine. Besides answering critical questions like the direction of cell differentiation, neo-vascularization, and the construction of functional, macroscopic tissue structures, the aim is to develop a concept that meets the increasing demand for bioartificial tissues and organs.

To this end, a concept was developed by the Fraunhofer Life Sciences Alliance together with the Fraunhofer Production Alliance, in order to provide an interdisciplinary overview and working arena to integrate the progressing scientific knowledge in the field with the development of production processes. The end goal is the mass production of tissue products. Besides Fraunhofer IZI, four other Fraunhofer institutes are cooperating on "Zellwerk".

Transplantation Tolerance

The federal ministry of education and research has funded a junior research group developing new strategies for the induction of specific immune tolerance in cell therapy and organ transplants. The term "immune tolerance" refers to donor-specific "non-reactivity" to foreign tissue occurring even though the defense function of the immune system to infection pathogens and malignant cells is maintained. Over the next two years, classical organ transplants will be augmented in hospitals by various cell therapy techniques. A critical issue is that a strategy is required which prevents foreign cells from being destroyed. For example, the question of immune tolerance needs to be solved in order to develop an islet cell transplant to treat Diabetes mellitus. In special animal models developed in Leipzig, human immune cells can be transferred to mice, triggering immunological defensive reactions. Systems like this can be used to test strategies that can then be transferred to common use.

Stem Cell Technology

The federal ministry of education and research has also funded a junior research group in stem cell technology. The main objectives of the group are to expand our knowledge of pluripotent stem cells and then develop techniques that can be transferred from the laboratory to the clinic. The results are expected to shed light on the molecular control of stem cell differentiation and cell aging and to research the potential for reprogramming somatic cell cores. Technologies are tested and developed that allow work on stem cells without the need for human ovary cells or violating German stem cell legislation. One particular goal is to develop disease-specific cell lines for pathogenesis research as well as for individual pharmacological and embryotoxicological drug testing.

Career Development

Internal Career Development

Introduction to Bioinformatics

Medical Product Law

Product Development for Medical Practice

GMP Training Program

Life Science Symposium

Seminar "Presentation Training"

Science Day and PhD Seminar

The staff of Fraunhofer IZI hold internal communication as a core value. This is reflected not only in common excursions and events, but also in the many scientific events held each year.

With this in mind, the doctoral candidates of the different working groups regularly present their work and progress in a seminar series. Besides the insight into the research topics and themes as well as the activities of other groups, the seminars provide the opportunity to discuss day-to-day problems with the larger community at the institute.

Twice a year, the institute organizes Science Day during which all of the working groups present their most important projects and network about common challenges and problems.

External Career Development

13th International Congress of Immunology
IUIS, Rio de Janeiro, Brazil

2nd User Meeting "LightCycler® 480"
Roche Diagnostics, Fulda

Annual European Congress of Rheumatology
EULAR, Barcelona, Spain

Annual Meeting of the Society of Hematology
ASH, Atlanta, USA

Working Group "Clinical Immunology"
DGfI, Frankfurt

Autumn Meeting
AVA/ECVA, Leipzig

Reviewer Experience Exchange
ZLG, Bonn

Comprehensive analysis of Affymetrix Exon expression data using BioConductor
ISCB, Vienna, Austria

Dresdner Symposium on Autoantibodies
GFID, Dresden

Introduction to Flow Cytometry
Becton Dickinson, Heidelberg

Introductory Seminar "Flow Cytometer FC500"
Beckmann Coulter, Krefeld

First Aid Course
DRK, Leipzig

Medical Specialty Development Course "Internal Medicine"
IKIT, Leipzig

Spring Conference
DGK, Mannheim

Skin Transplantation – Small Rodents
Charité, Berlin

Industrial Production of Biomolecules
GE Healthcare, Leipzig

InterNeuro Research Training Group
University of Leipzig

Annual Conference of the German Association for Hematology and Oncology
DGHO, Basel, Switzerland

Annual Conference
DGfZ, Regensburg

Communications Seminar
WSR, Leipzig

Crisis Management/Crisis PR
BPI/FhG, Munich

Course on "Image Processing and Visualization"
University of Leipzig, TRM, Leipzig

NeuroScience Conference "What's Wrong With My Mouse? Strategies for Rodent Behavioral Phenotyping"
San Diego, USA

Patent Workshop
German Patent and Trademark Office, Leipzig

Phadia Forum
Phadia, Stuttgart

Postgraduate Qualification "Immunologie"
bib, Leipzig

Postgraduate Course (PGS) "Toxicology und Environmental Protection"
University of Leipzig

Project Management I
WSR, Hamburg

Project Management II
WSR, Hamburg

Quality Management in Cell Culture
PromoCell, Heidelberg

Seminar "Protein Analysis"
GE Healthcare, Brunswick

Veterinary Medicine Training "BPT-Conference"
German Association of Veterinarian General Practitioners, Bremen

Animal Experiment Course
University of Leipzig

Training "ChIP-on-chip"
NIMR London, UK

Workshop "Column Validation"
GE Healthcare, Munich

XVII Conference on Horse Diseases and Stem Cell Therapy in Veterinary Medicine
Animal Hospital Hochmoor, Essen

Teaching Activities

University of Leipzig

Allergy in QSB4 Immunology	L
Allergy in QSB4 Immunology	L
Autoimmunity	L
Biotechnology	L
Clinical Immunology	L
Clinical Immunology for Dentists	L
Disease Models in Biomedical Research	L
English in Medicine	PBL
Graft versus Host Disease	L
Immunology	P
Immunology for Medics	L
Immunology and Cell Biology	F
Infection and Immunity	PBL
Interdisciplinary Subject: Infection and Immunity	C
Molecular Diagnostics	L
Perspectives of Auto-antibody Diagnostics	L
Postgraduate Qualification – Immunology	F
Preclinic I, Regenerative Medicine	L
QSB4 Immunology	C
Regenerative Medicine	L
Seminars for doctoral students	S
Stem Cell Differentiation	L/P
Therapeutic Protein Production	L
Therapy with Adult Stem Cells	L
Transfusion Medicine	L

Fraunhofer Institute for Cell Therapy and Immunology

Introduction to Bioinformatics	L/C

Leibniz Forum

Ethics & Stem Cells	L

Wilhelm Ostwald School, Leipzig

Tutor BELL Project	L

bib-group outplacement GmbH, Leipzig

Specialist in Biotechnology	F
bib-Bio-course	F/P

Donau-University Krems

Stem Cells	L

L = Lecture or student training and teaching
S = Seminar
P = Practical training
C = Course
F = Further training
PBL = Problem-Based Learning

Association Memberships

American Association for the Advancement of Science
Dr. Jörg Baumann, Dr. Sabine Breun

American Heart Association
Dr. Alexander Deten

Working Group "TE-Erstattung des BMG"
Dr. Wilhelm Gerdes

Experimental Stem Cell Transplantation Study Group
Dr. Stephan Fricke

British Society for Research on Aging
Dr. Alexandra Stolzing

CellNet
Dr. Nicole zur Nieden

German Regenerative Medicine Society
Dr. Alexandra Stolzing, Scientific Advisory Board; Dr. Nicole zur Nieden

German Gerontology and Geriatric Society
Dr. Alexandra Stolzing

German Immunology Society (DGfI)
Dr. Jörg Lehmann, Dr. Sabine Breun; Representatives in the GLP-Commission, in Sector Committee 5 of the ZLG (Central Healthcare Bureau, Immunology Society), to the AML (Association of Medical Laboratory Companies, Immunology Society), to the AWMF (Association of the Scientific Medical Societies in Germany), Dr. Ulrich Sack

German Cardiology Society
Dr. Alexander Deten

Germany Pharmaceutical Society (DPhG)
Catharina Frey-Duisberg

German Physiology Society
Dr. Alexander Deten

German Association of Universities and Colleges
Dr. Ulrich Sack

European Autoimmunity Standardization Initiative (EASI)
Dr. Ulrich Sack, Coordinator of the German Group

European Society of Cardiology
Dr. Alexander Deten

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

Future Virology
Dr. Jörg Baumann, Reviewer

German Neuroscience Society
Dr. Wilhelm Gerdes

German Gerontology Society
Dr. Alexandra Stolzing

German Society for Clinical Chemistry and Laboratory Medicine
Dr. Ulrich Sack, Flow Cytometry and Quantitative Microscopy Study Group

Society for Stem Cell Research
Dr. Alexandra Stolzing

Society for Laboratory Animal Studies (GV-SOLAS)
Dr. Jörg Lehmann

Society for Virology
Dr. Jörg Baumann

Cytometry Society
Dr. Ulrich Sack, Scientific Advisory Board

Association for the Advancement of Immune Diagnostics (GFID)
Dr. Manja Kamprad, Founding Member

Association for the Advancement of Immune Diagnostics (GFID)
Dr. Ulrich Sack, Member, Executive Committee

Institutional Review Board and Stem Cell Research Oversight Committee, StemCore
Dr. Nicole zur Nieden, Alternate member

International Society for Stem Cell Research
Dr. Nicole zur Nieden

International Society of Heart Research
Dr. Alexander Deten

International Study Group for Stem Cell Therapy (ISGSCT)
Dr. Nicole zur Nieden, Selected member

ISCB
Dr. Jörg Hackermüller

Journal of Biological Chemistry
Dr. Jörg Baumann, Reviewer

Journal "Future Drugs – Expert Reviews Vaccines"
Dr. Jörg Lehmann, Reviewer

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

Journal "Veterinary Immunology and Immunopathology"
Dr. Jörg Lehmann, Reviewer

NIH Immunology Interest Group
Dr. Jörg Baumann, Sabine Breun

NIH Virology Interest Group
Dr. Jörg Baumann, Dr. Sabine Breun

PLOS one
Dr. Jörg Baumann, Reviewer

Society for Developmental Biology
Dr. Nicole zur Nieden

Society for Neuroscience
Johannes Boltze, Daniel-Christoph Wagner, Alexander Kranz, Doreen Reich, Uwe Schmidt, Björn Nitzsche

Student Society for Stem Cell Research
Dr. Nicole zur Nieden, Chair, Research & Industry Committee

Translational Centre for Regenerative Medicine Leipzig
Dr. Wilhelm Gerdes, Advisory Board Member

Virology
Dr. Jörg Baumann, Reviewer

Wellcome Trust Global Research Alliance
Dr. Sonya Faber

Student Competitions

TSA – Wilhelm Ostwald School

Fraunhofer IZI continued its support of the students of the Technology Student Association (TSA) at the Wilhelm Ostwald School in Leipzig. The TSA is a US organization whose motto is, "Learning to live in a technical world." Every year it hosts an international science competition for teams of students. The TSA group of the Ostwald School is unique in Europe and has participated in the final competitions in the USA, without national preselections of competing teams. The "Ostwaldianer" have repeatedly earned this privileged place at the top through consistent high-level performance. This year, scientists from Fraunhofer IZI supervised three projects of the TSA-Ostwald team. In student practical trainings and research seminars, students explored topics like "Protein Analysis of Organs," "Research and Development of Stem Cells," and "Treatment of Stroke with Stem Cells." Besides a scientific essay, visual representation of the topics stands in the forefront of the multifaceted projects.

In the coming year, Fraunhofer IZI will again support interested students in this endeavor. Projects will begin already in spring 2008.

REGMED50

The institute is developing its activities in support of scientifically interested students with the student competition REGMED50. Secondary students were invited to present their visions of "Regenerative Medicine in 50 Years." Different formats were accepted for the presentation of their ideas of the future of regenerative medicine. The winner was invited to the 3rd WCRM and was also recognized during the presentation of the poster prizes. The picture "Leben durch Selbstmord" ("Life through Suicide"; see also the cover image) by Tina Kopetzky of the Geschwister-Scholl-Gymnasium in Taucha was selected by the jury as first place. The prize was a multi-week practical training at the institute as well as a non-cash prize.

Events

Prof. Dr. Bernat Soria Escoms being interviewed.

From left to right: Prof. Dr. Bernat Soria Escoms, Prof. Dr. Frank Emmrich, Prof. Dr. Dietmar Hutmacher, Prof. Dr. Heike Mertsching.

3rd World Congress on Regenerative Medicine (WCRM)

Regenerative medicine (from lat. *regeneratio* = produce again) is a comparatively new field in biomedicine. It addresses the healing of various diseases by the regeneration of malfunctioning cells, tissues and organs by means of biological replacement, for example, using engineered tissue or by stimulating the endogenous regeneration or repair processes. Therefore, behind the term, "regenerative medicine," one finds many different disciplines. Medics, scientists and engineers must work closely together. The goal is the discovery and comprehension of the processes in cell, tissue and organ function and on that basis, to develop therapies. Regenerative medicine uses information from many disease profiles, like organ failure, organ impairment, trauma and age-related deterioration. This combination of interdisciplinary knowledge and experiences has become an irreplaceable tool for research in the field. Events like the WCRM make significant contributions to the field by bringing researchers from the different sectors together to exchange experiences and to find common solutions through networking.

The goal of this congress was to unite the interdisciplinary research arms under one roof and to discuss the newest findings of scientists from around the world. However, the congress did not only serve scientific exchange, but also included a number of presentations on regulatory affairs, legal aspects and industrial perspectives that contributed significant and necessary insights into the respective fields and thereby strengthened the relationships between science, politics and economics. The congress also serves to engage the public by creating a forum for interested laypeople to gain a comprehensible look into the science of regenerative medicine.

The main topics of the congress were:
- stem cells
- immunology
- tissue engineering
- metabolism
- biomaterials und scaffolds
- imaging
- regulation
- industry symposia

With nearly 1000 participants from 33 nations, the 3rd World Congress set a new participant record. The accompanying industry exhibition, with its more than 60 exhibitors, demonstrated clearly the industrial interest in regenerative medicine.

In 50 sessions, 205 presentations were given by established scientists as well as relative newcomers. The international presenters included, for example, stem cell expert Mahendra Rao, vice president of stem cell research at the American company, Invitrogen. He spoke about the work with human embryonal stem cells and their theoretic infinite regenerative potential.

Opening Ceremony Panel (left to right): Prof. Dr. Bernat Soria Escoms, Dr. Klaus Theo Schröder, Dr. Peter Lange, Jörg Geiger.

Get together in the Congress Center Leipzig.

On the topic of non-coding RNAs, participants heard from one of the leading experts, Tom Gingeras, from Affymetrix, also an American company. Other top-notch referees were Chris Mason who presented on the state of regenerative medicine and Dietmar Hutmacher who works and researches on tissue engineering in Singapore.

The 230 submitted posters that were exhibited contributed additionally to the scientific program. The three best posters were recognized at the close of the congress with poster prizes. The breaks as well as the evening events were intensely used by the participants to engage in both scientific and commercial dialog. In this relaxed atmosphere, the opportunity to discuss cooperations and to network was optimized.

The Spanish minister for health and consumer protection, Professor Bernat Soria Escoms, himself a renowned stem cell researcher, emphasized the importance of translation – both bringing therapy concepts to the patients and at the same time across borders – and thus the cooperation of all European states in the field of regenerative medicine. In his presentation, Professor Soria Escoms spoke about stem cell research in diabetes.

Regarding research activities in the field of embryonal stem cells, the German research scene called for a more liberal control. "We must not lose the connection to international research due to too strong of restrictions," emphasized Congress President, Professor Emmrich.

The ever-increasing participant numbers support the fact that the World Congress has established itself as an internationally renowned scientific event. It will also be necessary, in the future, to bring the widespread interdisciplinary fields together, in order to seek out and recognize innovative solutions to the problems in the field. The industry presence is also important – particularly to research areas that are close to the clinic – due to their role in translating market-ready products.

In 2009 the WCRM will return to Leipzig. The PST/Fraunhofer IZI and its partners are already working on the plans for the fourth event in this series.

Conventions and Conferences

12th Leipziger Workshop "Cytomics and translational medicine"
19.-21.4.2007, Leipzig O/P

17th Annual Meeting of the German Society of Cytometry
10.-13.10.2007, Regensburg O

22nd TBI Winter Seminar
18.-24.2.2007, Bled, Slovenia O

2nd Congress of the German Society for Stem Cell Research
4.-6.10.2007, Würzburg P

2nd Fraunhofer Life Science Symposium
17.10.2007, Leipzig O

3rd World Congress on Regenerative Medicine
18.-20.10.2007, Leipzig P/O/S

33rd Congress of the German Society for Rheumatology
19.-22.9.2007, Hamburg P

37th Annual Conference of the German Society for Immunology
5.-8.9.2007, Heidelberg P/O

3rd International Workshop on Concepts and Mathematical Models of Stem Cell Organization
24.-26.9.2007, Machern O

3rd Symposium of the Zurich Center for Integrative Human Physiology ZIHP
31.8.2007, Zürich, Switzerland O

48th International Meeting, German Society of Pharmacology & Toxicology
13.-15.3.2007, Mainz O

5th Workshop "Transplantation Immunology" of the Working Group on Transplantation Immunology
20.-21.4.2007, Leipzig O

5th International Congress of Cardiology on the Internet
1.9.-30.11.2007, Buenos Aires, Argentina O

6th Leipziger Research Festival for Life Sciences
14.12.2007, Leipzig P

86th Annual Meeting of the German Physiological Society
25.-28.5.2007, Hanover O

AAI
18.- 22.5.2007, Miami, USA S

Abcam 2nd Stem Cell Symposium
13.-16.12.2007, Punta Cana, Dominican Republic O

Annual Meeting of the Society for NeuroScience
3.-7.11.2007, San Diego, USA P/O

Ausbiotech 2007
21.-24.10.2007, Brisbane, Queensland, Australia S

Autumn Meeting of the European College of Veterinary Anesthesia (ECVA) and of the Association
19.-21.9.2007, Leipzig O

BIO 2007
6.-9.5.2007, Boston, USA S

BioJapan
19.-21.9.2007, Yokohama, Japan P/O

Biotechnika
9.-11.10.2007, Hanover S

BMBF BioFuture
28.-29.1.2007, Berlin P

BMBF-Competition Biofuture
29.-30.1.2007, Berlin P

Brain´07 and BrainPET´07
20.-24.5.2007, Osaka, Japan P

DGHO
5.-9.10.2007, Leipzig P

Fall Seminar of IZBI Leipzig
29.-31.10.2007, Cesky Kamenice, Czech Republic O

HESI Workshop on Alternative Assays for Developmental Toxicity
27.-28.2.2007, Cary, NC, USA O

Hypoxia – from Integrative Biology to Human Disease
25.-30.11.2007, Monte Veritá, Switzerland P

IBIDA, 21st Annual Conference
11.-12.10.2007, Oakbrook Terrace, IL, USA O

ISMB/ECCB
21.-25.7.2007, Vienna, Austria P

Keynote Seminar
12.-17.4.2007, Snowbird, Utah, USA P

Keystone Symposium "MicroRNAs and Cancer"
8.-12.6.2007, Keystone, CO, USA P

L2L
8.5.2007, Leipzig P/O

Mini Symposium "Stem Cells for Skeletal Regeneration"
20.5.2007, Calgary, Canada O

Riboreg Workshop "Molecular Mechanisms Involving Non-Protein-Coding RNAs"
16.-18.3.2007, Carry-le-Rouet, France O

RNA 2007, Twelfth Annual Meeting of the RNA Society
29.5.-5.6.2007, Madison, WI, USA P

Saxon Biotechnology Day
28.11.2007, Dresden P

Second All-European Dyslexia Conference
15.-17.11.2007, Luxemburg O

SENS III
26.-30.8.2007, Cambridge, UK P/O

STEPS Meeting
26.-27.10.2007, Washington, USA O

Tissue aging: from molecular biology to clinical perspectives
20.-23.9.2007, Halle O

Workshop on Transplantation Immunology of the German Society for Immunology
20.-21.4.2007, Leipzig O

P = Poster
O = Oral Presentation
S = Stand

Important Milestones

2nd Fraunhofer Life Science Symposium

The institute began organizing the international event series, Fraunhofer Life Science Symposium, in 2006. The premier was a full success and motivated the organization team for 2007. The second Fraunhofer Life Science Symposium was organized as a satellite symposium to the 3rd World Congress on Regenerative Medicine.

The event was dedicated to the special field of Tissue Regeneration in Veterinary Medicine. The large reception of this new topic was fully unexpected. Over 200 participants informed themselves in four sessions that included 14 presentations about the advances and relevance of regenerative medicine in veterinary medicine. Whether its stem cell technological, cell therapeutic, tissue engineering or immunological aspects, regenerative medicine is relevant to much more than just human medicine. To the contrary, veterinary medicine is not only of interest to regenerative medicine researchers due to the necessary animal experiments, but also because of the high demand for veterinary therapies, and the connected market potential. Thus, therapies or therapy concepts that have been developed for humans are being adapted and applied for the treatment of domestic animals and livestock.

In 2008, the event series will continue. The topic will be tissue regeneration in ischemic diseases.

For more information:
www.fs-leipzig.com

Prof. Dr. Frank Emmrich and Dr. Janez Potočnik.

EU-Commissioner Responsible for Science and Research Janesz Potočnik

On May 8, 2007 the EU-Commissioner for Science and Research, Dr. Janez Potočnik, visited Leipzig in connection with the "L2L – Sustainable Neighbourhood – From Lisbon to Leipzig" conference. Along with the minister president of Saxony, Professor Dr. Georg Milbradt, Dr. Potočnik visited the Fraunhofer Institute for Cell Therapy and Immunology (IZI).

At Fraunhofer IZI, the visitors were received by the institute's Director, Professor Dr. Frank Emmrich and led through the institute. The new building for Fraunhofer IZI was also viewed, which is a beneficiary of funds from the EU-Structure Fund. Dr. Gerno Schmiedeknecht explained the GMP facility and Dr. Jörg Baumann and Dr. Sabine Breun discussed their project with the EU-Commissioner, which is being supported by the renowned European Marie-Curie-Foundation.

Open Door Day on the Old Convention Center Grounds

On September 9, all doors were opened again on the Old Convention Center Grounds (Alte Messe) to welcome interested visitors and day-trippers. For the second time, the Fraunhofer IZI presented itself in the glass atrium of the BIO CITY. At the stand, researchers from the institute answered a stream of questions from visitors on themes from, "What does the Fraunhofer institute do?" to "What are stem cells and how can they be used to heal disease?" Additionally, Fraunhofer IZI staff from the GMP facility offered tours of the clean rooms and so had their hands full on this fine Sunday, as the interest in these tours

was huge. While the adults had Fraunhofer IZI's work explained to them, it wasn't boring for the little ones. They were invited to put their "hands-on" the model and test their knowledge about the human body and its organs. The "Kinderecke" provided an opportunity for them to get comfortable and watch a cartoon that entertainingly explained the composition and functions of our body.

Campus 2007

On Saturday, July 7, 2007 the campus event of the University of Leipzig was repeated with the "Marketplace of Sciences." In a stand-filled square, the many and varied scientific institutes in Leipzig introduced themselves to the public. The Fraunhofer Institute for Cell Therapy and Immunology, the Translational Centre for Regenerative Medicine (TRM), the BIO CITY and the Center for Biotechnology and Biomedicine (BBZ) shared a tent for this event. The motto for the group was, "The power of the cell! – What powers has a cell?" Visitors informed themselves about the Fraunhofer IZI-developed mouse model for stroke and could watch a film about the significance of stem cells.

The common project of all exhibitors in this tent was also well received. Many small and big artists left their imprint on T-shirts and enthusiastically drew the organs of the human body on the shirts – whether they were realist or abstract, they were definitely very creative. The scientists and staff of the participating institutions explained the different organs and their functions. Stem cells were viewable under a microscope that could, for example, differentiate into liver cells. The tent was often full to bursting with interested visitors – the biosciences of regenerative medicine were so exciting on that day!

Publications

Original Publications

Athanasius F, Bompfünewerer Consortium, Backofen R, Bernhart SH, Flamm C, Fried C, Fritzsch G, Hackermüller J, Hertel J, Hofacker IL, Missal K, Mosig A, Prohaska SJ, Rose D, Stadler PF, Tanzer A, Washietl S, Will S.
RNAs everywhere: genome-wide annotation of structured RNAs.
J Exp Zoolog B Mol Dev Evol. 2007; 308: 1-25.

Aupperle H, Garbade J, Schubert A, Barten M, Dhein S, Schoon HA, Mohr FW.
Effects of autologous stem cells on immunohistochemical patterns and gene expression of metalloproteinases and their tissue inhibitors in doxorubicin cardiomyopathy in a rabbit model.
Vet Pathol. 2007; 44(4): 494-503.

Brulport M, Schormann W, Bauer A, Hermes M, Elsner C, Hammersen FJ, Beerheide W, Spitkovsky D, Hartig W, Nussler A, Horn LC, Edelmann J, Pelz-Ackermann O, Petersen J, Kamprad M, von Mach M, Lupp A, Zulewski H, Hengstler JG.
Fate of extrahepatic human stem and precursor cells after transplantation into mouse livers.
Hepatology. 2007; 46: 861-870.

Brumme S, Arnold T, Sigmarsson H, Lehmann J, Scholz HC, Hardt WD, Hensel A, Truyen H, Roesler U.
Impact of Salmonella Typhimurium DT104 Virulence Factors invC and sseD affecting the onset, clinical course, colonization patterns and immune response of porcine salmonellosis.
Vet. Microbiol. in press.

ENCODE Project Consortium.
Identification and analysis of functional elements in 1% of the human genome by the ENCODE pilot project.
Nature. 2007; 447: 799-816.

Fangmann J, Wegmann C, Hoppe A, Martin P, Sack U, Harms J, Faber S, Emmrich F.
Characterization of dendritic cell subsets in patients undergoing renal transplantation.
Transplant Proc. 2007; 39: 3101-3104.

Förschler A, Boltze J, Waldmin D, Gille U, Zimmer C.
MRI of experimental focal cerebral ischemia in sheep.
Rofo. 2007 May; 179(5): 516-24.

Gebauer CM, Lenk H, Friedrich W, Sack U, Schuster V.
Severe clinical course of Wiskott-Aldrich-syndrome – clinical course, hematologic, immunologic and genetic findings.
Kinder- und Jugendmedizin. 2007; 7: 39-44.

Gessner C, Hammerschmidt S, Kuhn H, Hoheisel G, Gillissen A, Sack U, Wirtz H.
Breath Condensate nitrite correlates with hyperinflation in chronic obstructive pulmonary disease.
Respir Med. 2007; 101: 2271-2278.

Hau S, Reich DM, Scholz M, Naumann W, Emmrich F, Kamprad M, Boltze J.
Evidence for neuroprotective properties of human umbilical cord blood cells after neuronal hypoxia in vitro.
BMC Neuroscience, in press.

Haussig S, Schubert A, Mohr FW, Dhein S.
Sub-chronic nicotine exposure induces intercellular communication failure and differential down-regulation of connexins in cultured human endothelial cells.
Atherosclerosis. 2007; in press.

Hemdan NY, Emmrich F, Faber S, Lehmann J, Sack U.
Alterations of Th1/Th2 reactivity by heavy metals – Possible consequences include induction of autoimmune diseases.
Ann. N.Y. Acad. Sci. 2007; 1109: 129-137.

Hemdan NY, Lehmann I, Wichmann G, Lehmann J, Emmrich F, Sack U.
Immunomodulation by mercuric chloride in vitro: application of different cell activation pathways.
Clin. Exp. Immunol. 2007; 148: 325-37.

Hiemann R, Hilger N, Michel J, Nitschke J, Bohm A, Anderer U, Weigert M, Sack U.
Automatic analysis of immunofluorescence patterns of HEp-2 cells.
Ann N Y Acad Sci. 2007; 1109: 358-371.

Kaltenhauser S, Pierer M, Arnold S, Kamprad M, Baerwald C, Hantzschel H, Wagner U.
Anti-bodies against cyclic citrullinated peptide are associated with the DRB1 shared epitope and predict joint erosion in rheumatoid arthritis.
Rheumatology. 2007; 46: 100-104.

Kamprad M, Kindler S, Schuetze N, Emmrich F.
Flow cytometric immunophenotyping of umbilical cord and peripheral blood hematopoietic progenitor cells by different CD34 epitopes, CD133, P-glycoprotein expression and rhodamine-123 efflux.
Transfusion Medicine and Hemotherapy. 2007; 34: 195-203.

Kapranov P, Cheng J, Dike S, Nix DA, Duttagupta R, Willingham AT, Stadler PF, Hertel J, Hackermüller J, Hofacker IL, Bell I, Cheung E, Drenkow J, Dumais E, Patel S, Helt G, Ganesh M, Ghosh S, Piccolboni A, Sementchenko V, Tammana H, Gingeras TR.
RNA maps reveal new RNA classes and a possible function for pervasive transcription.
Science. 2007; 316: 1484-8.

Löffler D, Brocke-Heidrich K, Pfeifer G, Stocsits C, Hackermüller J, Kretzschmar AK, Burger R, Gramatzki M, Blumert C, Bauer K, Cvijic H, Ullmann AK, Stadler PF, Horn F.
Interleukin-6 dependent survival of multiple myeloma cells involves the Stat3-mediated induction of microRNA-21 through a highly conserved enhancer.
Blood. 2007; 110: 1330-3.

Meier H, Bullinger J, Deten A, Marx G, Rabald S, Zimmer HG, Briest W.
Tissue inhibitor of matrix metalloproteinase-1 in norepinephrine-induced remodeling of the mouse heart.
Cell Physiol Biochem. 2007; 20: 825-836.

Meng GL*, zur Nieden NI*, Liu SY, Cormier JT, Kallos MS, Rancourt DE.
Properties of murine embryonic stem cells maintained on human foreskin fibroblasts without LIF.
Mol Reprod Dev. 2007; Sept 20 [Epub ahead of print].
*Authors contributed equally to this study.

Rabald S, Hagendorff A, Pfeiffer D, Zimmer HG, Deten A.
Contrast enhanced echocardiographic follow-up of cardiac remodeling and function after myocardial infarction in rats.
Ultrasound Med Biol. 2007; 33: 1561-1571.

Saalbach A, Klein C, Sleeman J, Sack U, Kauer F, Gebhardt C, Averbeck M, Anderegg U, Simon JC.
Dermal fibroblasts induce maturation of dendritic cells.
Journal of Immunology. 2007; 178: 4966-4974.

Sack U, Bocsi J, Tarnok A.
Importance of cytometry for clinical diagnostics and therapy.
Transfus Med Hemotherapy. 2007; 34: 153-154.

Sack U, Conrad K, Csernok E, Frank I, Haass M, Krieger T, Seyfarth M, Schlosser U, Schmidt R, Witte T.
Standardization of autoimmune diagnostics in Germany: activities of the German group in the European Autoimmune Standardization Initiative.
Ann N Y Acad Sci. 2007; 1109: 31-36.

Sack U, Gerling F, Tarnok A.
Age-related lymphocyte subset changes in the peripheral blood of healthy children – A meta-study.
Transfus Med Hemotherapy. 2007; 34: 176-181.

Savkovic V, Gantzer H, Reiser U, Selig L, Gaiser S, Sack U, Kloppel G, Mossner J, Keim V, Horn F, Bodeker H.
Clusterin is protective in pancreatitis through anti-apoptotic and anti-inflammatory properties.
Biochem Biophys Res Commun. 2007; 356: 431-437.

Schloendorn J, Sethe S, Stolzing A.
Cellular therapy using microglial cells.
Rejuvenation Res. 2007 Mar; 10(1): 87-99.

Schwenk M, Sack U, Esser C, Klein R.
Diagnostic relevance of the determination of lymphocyte subpopulations in environmental medicine.
Int J Hyg Environ Health. 2007; 210: 177-198.

Sharma N, Kaur J, Xhu H, zur Nieden NI, Rancourt DE.
Characterization of secretory leukocyte protease inhibitor (SLPI) as an inhibitor of implantation serine proteinase.
Mol Reprod Dev. 2007 Dec 28 [Epub ahaed of print].

Stolzing A, Hescheler J, Sethe S.
Fusion and regenerative therapies: is immortality really recessive?
Rejuvenation Res. 2007 Dec; 10(4): 571-86.

Stolzing A, Jones E, McGonagle D, Scutt A.
Age related changes in human bone marrow-derived mesenchymal stem cells: consequences for cell therapies.
Mechanism of Ageing and Development. In press.

Tanneberger K, Kirchberger J, Bar J, Schellenberger W, Rothemund S, Kamprad M, Otto H, Schoneberg T, Edelmann A.
A novel form of 6-phosphofructokinase – Identification and functional relevance of a third type of subunit in pichia pastoris.
J Biol Chem. 2007; 282: 23687-23697.

Treese C, Lange F, Mittag A, Tarnok A, Loesche A, Emmrich F, Lehmann J, Sack U.
Characterization of fibroblasts responsible for cartilage destruction in arthritis.
Cytometry A. in press.

Washietl S, Pedersen JS, Korbel JO, Stocsits C, Gruber AR, Hackermüller J, Hertel J, Lindemeyer M, Reiche K, Tanzer A, Ucla C, Wyss C, Antonarakis SE, Denoeud F, Lagarde J, Drenkow J, Kapranov P, Gingeras TR, Guigó R, Snyder M, Gerstein MB, Reymond A, Hofacker IL, Stadler PF.
Structured RNAs in the ENCODE selected regions of the human genome.
Genome Res. 2007; 17: 852-64.

zur Nieden NI, Cormier JT, Rancourt DE, Kallos MS.
Murine embryonic stem cells maintain pluripotency after long-term culture in suspension bioreactors.
J Biotechnol. 2007; 129(3): 421-432.

zur Nieden NI, Price FD, Davis LA, Everitt R, Rancourt DE.
Gene array analysis on mixed ES cell populations: a biphasic role for beta-catenin in osteogenesis.
Mol Endocrinol. 2007; 21(3): 674-685.

Book Articles

Ackermann M, Kamprad M.
Qualitätskontrolle der Ac133-Depletion aus kryokonservierten mononukleären Zellen des Nabelschnurblutes.
Zelluläre Diagnostik. Grundlagen, Methoden und klinische Anwendungen der Durchflusszytometrie. Hrsg.: Sack u, Tarnok A, Rothe G. KARGER Verlag, Freiburg, 2007, 867-886.

Fricke S.
Acute Graft versus Host Disease (aGvHD) in a triple transgenic mouse model.
Abstract Book 2007, 6th Leipzig Research Festival for Life Sciences. Band 1.
Hrsg.: Thiery J, Beck-Sickinger A, Arendt T.
K. Plath Verlag, Leipzig, 2007, 165.

Lun A, Sack U.
Monitoring organtransplantierter Patienten.
Zelluläre Diagnostik.
Hrsg.: Sack U, Tarnok A, Rothe G.
Karger, Freiburg, 2007, 759-784.

Michel J, Hiemann R, Hilger N, Kaltschmidt K, Weigert M, Sack U, Anderer U.
HEp-2 cell preparation for automated analysis of autoantibodies.
From Etiopathogenesis to the Prediction of Autoimmune Diseases: Relevance of Autoantibodies.
Hrsg.: Conrad K, Chan EKL, Fritzler MJ, Sack U, Shoenfeld, Wiik AS.
Pabst, Lengerich, Berlin, Riga, Rom, Wien, Zagreb, 2007, 632-633.

Sack U, Gerling F, Tarnok A.
Lymphozyten im peripheren Blut gesunder Kinder.
Zelluläre Diagnostik.
Hrsg.: Sack U, Tarnok A, Rothe G.
Karger, Freiburg, 2007, 351-360.

Other Publications

Drexler J.
Zelltherapie gegen Parkinson.
FhG Mediendienst, 1/2007, Thema 1, S. 2-3.

Hackermüller J.
Genetischer Müll als Ordnungshüter.
Pressekonferenz, 2007 June 19

Hackermüller J.
Fernsehinterview.
Leipzig Fernsehen, 2007 June 19

Hackermüller J.
Invited Seminar, Nicht proteinkodierende RNA – die dunkle Materie der modernen Genomforschung.
Bioinformatics meets Life Science, 2007 March 6, Leipzig

Hackermüller J.
Invited Seminar: Universität Halle/Saale.
2007 September 20

Hackermüller J.
Radiointerview, RBB "Die Profis".
2007 June 23

Hackermüller J.
Service Gesundheit.
Fernsehinterview, SWR3, 2007 August 20

Hackermüller J.
Genetischer Müll als Ordnungshüter.
Presseinformation FHG, 2007 June 14

Hackermüller J.
Invited Seminar Osborne Memorial Laboratories.
Yale University, New Haven, CT, USA, 2007 June 5

Hackermüller J.
Wissen Hoch 12 – Erkenntnisse und Themen die uns bewegen 2007/2008.
Interview in Frater H, Podbregar N, Lohmann D, Springer 2007.

Horn F.
Invited Seminar: Die intrazelluläre Signaltransduktion im Zusammenspiel mit nicht-proteinkodierenden RNAs: eine neue Ebene der zellulären Regulation.
Bioinformatics meets Life Science, 2007 March 6, Leipzig

Kraft U.
Regenerieren statt reparieren.
Technology Review, 9/2007, S. 44-51.

Kretzschmar AK.
Invited Seminar: National Institute of Medical Research.
London, UK, 2007 October 29

Lehmann J.
Entwicklung des neuartigen automatischen Zellseparationssystems CellCelector zur Verleihung des Innovationspreises Thüringen an die Firma AVISO GmbH.
MDR-Fernsehbeitrag

Schmiedeknecht G.
Reinräume und Gerätetechnik bei der Zelltherapeutikaherstellung.
Contamination Control Report, 1, 2007, S. 44-47.

Schmiedeknecht G.
Erteilung Herstellungserlaubnis für EpiDex.
Pressemitteilung bei Bionity.com, 2007 October 30

Abstracts of Posters and Papers

Alfred R, Cormier JT, zur Nieden NI, Rancourt DE, Kallos MS.
Osteogenic differentiation of murine embryonic stem cells (mESCs) in suspension bioreactors.
57th Canadian Chemical Engineering Conference, 2007 October 28-31, Edmonton, Canada

Alfred R, Krawetz R, Cormier JT, zur Nieden NI, Rancourt DE, Kallos MS.
Suspension culture production of murine embryonic stem cell (ESC) derived osteoblasts: Effect of agitation and inoculation density.
Canadian Stem Cell Network, 6th Annual General Meeting, 2007 November 7-9, Toronto, Canada

Aupperle H, Garbade J, Schubert A, Dhein S, Mohr FW, Schoon HA.
Injection of autologous mesenchymal bone-marrow derived stem cells in rabbits with chronic doxorubicin cardiomyopathy results in functional and histomorphological alterations of the cardiac extracellular matrix.
3rd World Congress on Regenerative Medicine, 2007 October 18-20, Leipzig; Reg Med 2, 525.

Aupperle H, März I, Thielebein J, Kiefer B, Kappe A, Schubert A, Schoon HA.
The role of MMPs and TIMPs in chronic valve disease (syn. endocardiosis) in dogs.
25th Annual Meeting of ESVP, 2007 August 29-September 1, München; Tagungsband S. 52.

Barthel H, Boltze J, Förschler A, Großmann U, Schildan A, Boltze CM, Gille U, Patt M, Seese A, Becker G, Emmrich F, Sabri O.
Brain perfusion and glucose consumption PET to monitor stem cell effects on stroke outcome in a new large animal model – A feasibiliy study.
Annual meeting of the European Associatoin of nuclear medicine, 2007 October 13-17, Copenhagen, Denmark

Barthel H, Boltze J, Großmann U, Schildan A, Förschler A, Gille U, Patt M, Seese A, Emmrich F, Sabri O.
A feasibility study on quantitative [15O] H2O and [18F] FDG brain PET in a new large-animal stroke model in sheep.
Brain´07 and BrainPET´07, 2007 May 20-24, Osaka, Japan

Bold A, Wurth R, Keller T, Trahorsch U, Voigt P, Schubert S, Sack U.
Evaluation and validation of a manual low-cost assay for the monitoring of CD4 counts in HIV-infected individuals in non-OECD countries.
12th Leipziger Workshop "Cytomics and translational medicine", 2007 April 19-21, Leipzig; Cytometry A, 71 (2007) 525.

Boltze J, Förschler A, Barthel H, Lang AB, Boltze CM, Sabri O, Emmrich F, Gille U.
Permanent MCAO in sheep – a novel model of focal cerebral ischemia.
Brain´07 and BrainPET´07, 2007 May 20-24, Osaka, Japan

Boltze J, Förschler A, Boltze CM, Nitzsche B, Barthel H, Emmrich F, Gille U.
Multimodal evaluation of autologous bone marrow cell therapy of stroke in a large animal trial.
3rd World Congress on Regenerative Medicine, 2007 October 18-20, Leipzig

Boltze J, Förschler A, Schmidt UR, Wagner,DC, Schwarz J, Boltze CM, Bulawina L, Lang AB, Barthel H, Sabri O, Emmrich F, Gille U.
Cell Therapy of stroke in small and large animals.
Brain´07 and BrainPET´07, 2007 May 20-24, Osaka, Japan

Boltze J, Nitzsche B, Förschler A, Boltze CM, Reischauer A, Hoffmann A, Geiger K, Barthel H, Härtig W, Gille U.
Multimodal evaluation of autologous bone marrow cell therapy of stroke in a large animal trial.
NeuroScience Conference, 2007 November 3-7, San Diego, USA

Boltze J.
Development of Novel Stroke Therapies – translational research from bench to bedside.
BioJapan, 2007 September 19-21, Yokohama, Japan

Boltze, J.
Autologous cell therapy of stroke in a novel large animal model of focal cerebral ischemia.
The STEPS meeting, 2007 Oktober 27-28, Arlington, USA

Borte St, Liebert UG, Borte M, Sack U.
MMR-vaccination in children with juvenile idiopathic arthritis treated with methotrexate and etanercept.
Z. Rheumatol. 66, 2007, 627.

Cormier JT, Kallos MS, Rancourt DE, zur Nieden NI.
Three-dimensional culture of ESCs enhances their osteogenic and chondrogenic differentiation potential.
Keynote seminar: Tissue Engineering and Developmental Biology, 2007 April 12-17, Snowbird, Utah, USA

Cormier JT, zur Nieden NI, Krawetz RJ, Kallos MS, Rancourt DE, Matyas JA.
Assessing the efficacy of stem cells for tissue repair in a skeletal defect model.
Canadian Arthritis Network 2007, Annual Scientific Conference, 2007 October 11-13, Halifax, Canada

Cormier JT, zur Nieden NI, Krawetz RJ, Matyas JR, Rancourt DE.
Osteogenic differentiation of embryonic stem cells reduces the risk of teratoma formation in vivo.
Canadian Stem Cell Network, 6th Annual General Meeting, 2007 November 7-9, Toronto, Canada

Dao L, Stolzing A.
Fusion mediated regeneration of cells using adult stem cells.
3rd World Congress on Regenerative Medicine, 2007 October 18-20, Leipzig

Dao L, Stolzing A.
Stem cell fusion and aging.
SENS III, 2007 August 6-10, Cambridge, UK

Dunker K, Baumann JG, KewalRamani VN, Emmrich F, Breun SKJ.
C-type lectins and the regulation of the immune system.
3rd World Congress on Regenerative Medicine, 2007 October 18-20, Leipzig

Dunker K, Baumann JG, KewalRamani VN, Emmrich F, Breun SKJ.
DC-SIGN and the regulation of HIV transmission to T cells.
6th Leipzig Research Festival for Life Sciences, 2007 December 13-14, Leipzig

Emmrich F, Boltze J, Lesny P, Gerdes W, Zilch C, Faber S, Hajek M, Sykova E.
Nano4Brain and Nerves: The Use of Nanotechnology in Neuronal Repair for both improved Quality of Life and Long-Term Outcomes through Stimulation of Endogenous Regeneration.
L2L Lissabon to Leipzig, 2007 May 7-8

Faber S, Boltze J, Barthel H, Linke A, Hengstler JG.
Review of the First Fraunhofer Life Science Symposium on Cell Therapy and Immunology – October 22-24, 2006, Leipzig, Germany.
EXCLI Journal. 2006; 5: 217-225 – ISSN 1611-2156.

Fasold M, Brücker J, Stadler PF, Binder H, Hackermüller J.
A new program package for model-based microarray analysis.
3rd World Congress on Regenerative Medicine, ncRNA workshop, 2007 October 18-20, Leipzig

Fricke S, Ackermann M, Blaschke R, Lehnert S, Uharek L, Ruschpler P, Braun JM, Emmrich, F.
Establishing a transplantation model for the induction of xenogenic GvHD in mice: An animal model for studying potential therapeutic strategies to prevent Graft-versus-Host Disease (GvHD).
BMBF-Wettbewerb BioFuture, 6. Präsentation, 2007 January 29-30, Berlin

Fricke S, Hilger N, Ackermann M, Uharek L, Hildebrandt G, Jahns J, Braun JM, Emmrich, F.
Acute Graft versus Host Disease (aGvHD) in a MHC-II humanised triple transgenic mouse model: advantages for testing new therapeutic strategies?
DGHO, 2007 October 4-9, Basel, Switzerland

Fricke S, Hilger N, Ruschpler P, Ackermann M, Uharek L, Hildebrandt G, Jahns J, Braun JM, Emmrich F.
A humanised triple transgenic mouse model: Induction of acute GvHD and the effects of X-Rays and chemotherapy on hematopoiesis.
3rd World Congress on Regenerative Medicine, 2007 October 18-20, Leipzig

Fricke S, Hilger N, Ruschpler P, Ackermann M, Uharek L, Hildebrandt G, Jahns J, Braun JM, Emmrich, F.
Induction of xenogenic acute Graft versus Host Disease (aGvHD) in mice.
Annual Meeting German Society of Immunology, 2007 September 4-7, Heidelberg

Fricke S, Hilger N, Ruschpler P, Ackermann M, Uharek L, Hildebrandt G, Jahns J, Braun JM, Emmrich, F.
Induction of xenogenic acute Graft versus Host Disease (aGvHD) in mice.
Workshop Transplantation, Immunology German Society of Immunology, 2007 April 20-21, Leipzig

Geßner C, Rechner B, Koker J, Kuhn H, Hammerschmidt S, Gillissen A, Hoheisel G, Sack U, Wirtz H.
Erhöhte Konzentrationen von VEGF, bFGF und Angiogenin im Atemkondensat bei Patienten mit einem nichtkleinzelligen Lungenkarzinom (NSCLC).
Pneumologie 61 (2007) P108.

Hackermüller J, Löffler D, Brocke-Heidrich K, Pfeifer G, Fried C, Kretzschmar AK, Ullmann K, Burger R, Gramatzki M, Blumert C, Bauer K, Cvijic H, Stadler PF, Horn F.
Identification of Stat3 controlled miRNAs involved in oncogenesis.
RNA 2007, 12th annual meeting of the RNASociety, 2007 May 29-June 3, Madison, WI, USA; Book of abstracts: 176.

Hanisch I, Stolzing A.
Fusion and cellular reprogramming.
Sächsischer Biotechnologietag, 2007 November 28, Dresden

Hemdan N, Lehmann J, Emmrich F, Faber S, Sack U.
Induction and/or exacerbation of autoimmune disorders by heavy metals may be mediated by changing cytokine levels.
6th Leipzig Research Festival for Life Sciences, 2007 December 13-14, Leipzig

Hemdan N, Lehmann J, Emmrich F, Sack U.
Possible induction or exacerbation of autoimmune diseases by heavy metals through changing cytokine profiles.
37th Annual meeting of the German Society of Immunology (DGfI), 2007 September 5-8, Heidelberg

Hiemann R, Hilger N, Weigert M, Sack U, Michel J, Anderer U.
Image based description of immunofluorescence on HEp-2 cells.
Cytometry A, 71 (2007), 60.

Hoffmann S,Stadler PF, Hackermüller J.
Relaxed alignments: a fast mapping method for next-generation sequencing data.
3rd World Congress on Regenerative Medicine, ncRNA workshop, 2007 October 18-20, Leipzig

Huber C, Gassmann M, Deten A.
Right ventricular and pulmonary response to acute hypoxia in erythropoietin-overexpressing mice.
3rd Symposium of the Zurich Center for Intergrative Human Physiology ZIHP, 2007 August 31, Zürich, Switzerland

Huber C, Hu J, Soliz J, Mihov D, Gorr T, Gassmann M, Deten A.
Right ventricular and pulmonary response to acute hypoxia in erythropoietin-overexpressing mice.
Hypoxia, from Integrative Biology to Human Disease, 2007 November 25-30, Monte Veritá, Switzerland

Kim M, zur Nieden NI, Loken SD, Urbanski SJ, Lee PWK, Rancourt DE, Johnston RN.
Safety of attenuated reovirus on the developmental potential of embryonic stem cells.
Mayo Clinic Oncolytic Virus Conference, 2007 March 14-17, Scottsdale, AZ, USA

Knauer J, Siegemund S, Müller U, Al-Robaiy S, Lehmann J, Kastelein RA, Alber G, Straubinger RK.
Borrelia burgdorferi potently activates bone marrow-derived conventional dendritic cells for production of IL-23 required for IL-17 release by T-cells.
Proceedings of the 3rd World Congress on Regenerative Medicine, 2007 October 18-20, Leipzig

Kretzschmar AK, Michel M, Stadler PF, Horn PF, Kerstin U, Schulz C, Hackermüller J.
RNA-RNA interactions in living cells: Development of efficient high throughput methods to unhide the multiple targets of miRNAs.
RNA 2007, 12lth annual meeting of the RNASociety, 2007 May 29-June 3, Madison, WI, USA; Book of abstracts: 321.

Kretzschmar AK, Michel M, Ullmann K, Schulz C, Stadler PF, Horn F, Hackermüller J.
Development of methods to unhide the multiple targets of miRNAs.
Keystone Symposium "MicroRNA and Cancer", 2007 June 8-12, Keystone, CO, USA

Kuhn H, Hammerschmidt S, Sack U, Geßner C, Gillissen A, Wirtz H.
Mechanische Dehnung mit hoher Amplitude modifiziert die Freisetzung von Zytokinen und Prostanoiden aus alveolären Typ II Zellen.
Pneumologie 61 (2007).

Kuske B, Trettner S, zur Nieden NI.
Enrichment of mesenchymal progenitors from embryonic stem cells.
3rd World Congress on Regenerative Medicine, 2007 October 18-20, Leipzig

Lange F, Bajtner E, Rintisch C, Nandakumar KS, Sack U, Holmdahl R.
Action of methotrexate in various models of RA and MS is dependent on T-cell activation.
J. Immunol. 176 (2007), S. 147.

Nitzsche B, Förschler A, Boltze CM, Reischauer A, Hoffmann A, Geiger K, Barthel H, Härtig W, Gille U, Boltze, J.
Stroke in sheep – multimodal evaluation of a novel large animal model of focal cerebral ischemia.
NeuroScience Conference, 2007 November 3-7, San Diego, USA

Prenzel F, Gebauer C, Hügle B, Schille R, Sack U, Hirsch W, Schuster V.
14 Jahre altes Mädchen mit isolierter autoimmuner Lungenerkrankung: atypischer Lupus erythematodes?
11. Interdisziplinäres Kinderimmunologisches Arbeitstreffen, 2007 October 26, Höfgen-Kaditzsch

Rabald S, Marx G, Mix B, Stephani C, Kamprad M, Cross M, Boltze J, Zimmer HG, Deten A.
MN-CBCS or USSCS do not improve survival or heart function but modulate remodeling after myocardial infarction in rats.
12. Leipziger Workshop Cytomics and Translational Medicine Incorporating: 5th International Workshop, Slide-Based Cytometry, 2007 April 19-21, BIO CITY Leipzig; Cytometry A. 71A (7): 529-529 JUL 2007.

Rabald S, Marx G, Mix B, Stephani C, Kamprad M, Cross M, Bolze J, Zimmer H-G, Deten A.
Mononuclear cord blood cells (MN-CBCs) and unrestricted somatic stem cells (USSCs) do not improve heart function but extracellular re-modeling after myocardial infarction in rats.
5th International Congress of Cardiology on the Internet, 2007 September 1-November 30

Rabald S, Marx G, Mix B, Stephani C, Kamprad M, Cross M, Bolze J, Zimmer HG, Deten A.
Mononuclear cord blood cells (MN-CBCs) and unrestricted somatic stem cells (USSCs) do not improve heart function but extracellular re-modeling after myocardial infarction in rats.
86. Jahrestagung der Deutschen Physiologischen Gesellschaft, 2007 March 25-28, Hannover; Acta Physiologica; 189 (Suppl 653); O09-3.

Reich DM, Hau S, Kamprad M, Boltze J.
Neuronal hypoxia: protective effects of mononuclear cord blood cells after direct and indirect application.
2nd Congress of the German Society for Stem Cell Research, 2007 October 4-6, Würzburg

Reich DM, Hau S, Kamprad M, Scholz M, Emmrich F, Boltze J.
Preventing hypoxic brain damage: effects of direct and indirect stem cell administration in a new culture model of the penumbra.
Brain´07 and BrainPET´07, 2007 May 20-24, Osaka, Japan

Reich DM, Hau S, Naumann W, Emmrich F, Kamprad M, Boltze J.
Mononuclear vs. AC133+ cord blood cells for experimental stroke therapy – evaluation of neuroprotective properties in vitro and in vivo.
NeuroScience Conference, 2007 November 3-7, San Diego, USA

Reich DM, Hau S, Naumann W, Emmrich F, Kamprad M, Boltze J.
Neuronal hypoxia: protective effects of mononuclear cell fractions after direct and indirect application.
3rd World Congress on Regenerative Medicine, 2007 October 18-20, Leipzig

Reich DM, Hau S, Naumann W, Emmrich F, Kamprad M, Boltze J.
Neuronal hypoxia: protective effects of mononuclear cell fractions after direct and indirect application.
6th Leipzig Research Festival for Life Sciences, 2007 December 13-14, Leipzig

Reichert D, Richter F, Sack U, Kuhn H, Geßner C, Hammerschmidt S, Wirtz H.
Einfluss der n-CPAP Therapie auf die bronchiale Entzündung bei Patienten mit einem schweren Schlafapnoesyndrom.
Pneumologie 61, 2007.

Reischauer A, Nitzsche B, Boltze J, Gille U, Förschler A, Barthel H, Schoon HA.
Stroke – the development of a large animal model with sheep for a better scientific and therapeutic understanding.
Annual meeting of the European Society of Veterinary Pathology, 2007 August 29-September 1, München

Rose D, Hertel J, Reiche K, Stadler PF, Hackermüller J.
Duplicated RNA Genes In Teleost Fish Genomes.
3rd World Congress on Regenerative Medicine, ncRNA workshop, 2007 October 18-20, Leipzig

Rose D, Hertel J, Reiche K, Stadler PF, Hackermüller J.
ncDNAlign – a flexible and efficient package for the generation of non-protein coding multiple alignments from genomic sequences.
3rd World Congress on Regenerative Medicine, ncRNA workshop, 2007 October 18-20, Leipzig

Rose D, Hertel J, Reiche K, Stadler PF, Hackermüller J.
ncDNAlign – a flexible and efficient package for the generation of non-protein coding multiple alignments from genomic sequences.
ISMB/ECCB, 2007 July 21-25, Vienna, Austria

Saalbach A, Klein C, Sleeman J, Sack U, Kauer F, Gebhardt C, Averbeck M, Anderegg U, Simon JC.
Dermal fibroblasts induce maturation of dendritic cells.
Exp. Dermatol. 16 (2007), 211.

Sack U, Borte S, Hoppe A, Wegmann C, Luderer D, Oppel C, Bauer K, Emmrich F, Hauss J, Fangmann J.
Cytometric Monitoring of transplanted patients.
17th Annual Meeting of the German Society of Cytometry, 2007 October 10-13, Regensburg; Cytometry. 71 A (2007) 759.

Sack U, Lange F, Mittag A, Tarnok A, Hilger N, Lösche A, Emmrich F, Treese C.
Phenotypic characteristics of arthritic fibroblasts.
33. Kongress der Deutschen Gesellschaft für Rheumatologie, 2007 September 19-22, Hamburg; Z. Rheumatol. 66 Suppl. 1 (2007), 43.

Sack U.
Analysis of immune functions following solid organ transplantation.
12th Leipziger Workshop "Cytomics and translational medicine", 2007 April 19-21, Leipzig; Cytometry A. 71 (2007) 514.

Sack U.
Analysis of immune functions following solid organ transplantation.
5. Workshop "Transplantationsimmunologie" des Arbeitskreises Transplantationsimmunologie der Deutschen Gesellschaft für Immunologie, 2007 April 20-21, Leipzig

Sack U.
Bead based cytometry: selected applications.
17th Annual Meeting of the German Society of Cytometry, 2007 October 10-13, Regensburg; Cytometry. 71 A (2007) 749.

Sack U.
Immundefekte und Immundefizienz – Wie häufig? Wie messbar? Wie therapierbar? Aktuelle pneumologische Infektiologie in Praxis und Klinik.
2007 January 20, Leipzig

Sack U.
Immunologisches Transplantatmonitoring.
11. Interdisziplinäres Kinderimmunologisches Arbeitstreffen, 2007 October 26, Höfgen-Kaditzsch

Sack U.
Immunomodulatory effects of anesthesia and surgical trauma.
Autumn Meeting of the European College of Veterinary Anaesthesia (ECVA) and of the Association of Veterinary Anaesthetists (AVA), 2007 September 19-21, Leipzig

Sack U.
In vitro-Diagnostik bei Arzneimittelreaktionen.
Weiterbildungsreihe der Klinik für Dermatologie, Universität Leipzig, 2007 January 31, Leipzig

Sack U.
Labordiagnostik allergischer Arzneimittelreaktionen.
5. Interdisziplinäres Leipziger Allergiegespräch, 2007 May 2, Leipzig

Sack U.
Molekulare Analytik und Diagnostik.
Fraunhofer IZI Science Day, 2007 September 10, Leipzig

Scherf N, Braumann UD, Kuska JP, Kamprad M, Sack U, Lange F.
Automatic analysis of cartilage regeneration in a model of human/murine SCID arthritis.
3rd World Congress on Regenerative Medicine, 2007 October 18-20, Leipzig; Regen. Med. 2 (2007), 678.

Schimmelpfennig C, Shurawel N, Emmrich F.
Cellular therapy with Cytokine induced killer cells (CIK cells) in patients with solid tumors.
3rd World Congress on Regenerative Medicine, 2007 October 18-20, Leipzig

Schmidt UR, Wagner DC, Förschler A, Kranz A, Bulawina L, Kamprad M, Egger D, Emmrich F, Boltze J.
Human Umbilical Cord Blood Cell treatment of stroke: MRI-controlled evaluation of the therapeutic time window.
NeuroScience Conference, 2007 November 3-7, San Diego, USA

Schmidt UR, Wagner DC, Förschler A, Kranz A, Bulawina L, Kamprad M, Egger D, Emmrich F, Boltze, J.
Intravenous administration of Human Umbilical Cord Blood Cells after stroke in rats: investigation of the therapeutic time window regarding functional recovery.
6th Leipzig Research Festival for Life Sciences, 2007 December 13 - 14, Leipzig

Schmidt UR, Wagner DC, Förschler A, Kranz A, Bulawina L, Kamprad M, Egger D, Emmrich F, Boltze, J.
Intravenous administration of Human Umbilical Cord Blood Cells after stroke in rats: investigation of the therapeutic time window regarding functional recovery.
3rd World Congress on Regenerative Medicine, 2007 October 18 - 20, Leipzig

Schulz C, Ullmann K, Feik S, Schreiber S, Schutt K, Stadler PF, Horn F, Hackermüller J, Kretzschmar AK.
Non-protein coding RNA (ncRNAs) knockdowns using short interfering RNAs (siRNAs): A proof of principle.
6th Leipzig Research Festival for Life Sciences, 2007 December 13 - 14, Leipzig

Schulz C, Ullmann K, Feik S, Schreiber S, Schutt K, Stadler PF, Horn F, Hackermüller J, Kretzschmar AK.
Non-protein coding RNA (ncRNAs) knockdowns using short interfering RNAs (siRNAs): A proof of principle.
3rd World Congress on Regenerative Medicine, ncRNA workshop, 2007 October 18 - 20, Leipzig

Schulz S, Schlegel R, Schulz C, Ullmann K, Stadler PF, Horn F, Hackermüller J, Kretzschmar AK.
Search for novel non-coding RNAs in prostate carcinoma cells.
3rd World Congress on Regenerative Medicine, ncRNA workshop, 2007 October 18 - 20, Leipzig

Schulz S, Schlegel R, Schulz C, Ullmann K, Stadler PF, Horn F, Hackermüller J, Kretzschmar AK.
Search for novel non-coding RNAs in prostate carcinoma cells.
6th Leipzig Research Festival for Life Sciences, 2007 December 13 - 14, Leipzig

Schuster V, Hügle B, Schille R, Sack U, Schwarz K, Schulz A.
6 Wochen alter männlicher Säugling mit MRSA-Staphylodermie: Wieviel Diagnostik ist erforderlich?
11. Interdisziplinäres Kinderimmunologisches Arbeitstreffen, 2007 October 26, Höfgen-Kaditzsch

Schutt K, Michel M, Ullmann K, Schulz C, Stadler PF, Mörl M, Horn F, Hackermüller J, Kretzschmar AK.
In vivo analysis of RNA-RNA interactions: Development of efficient high throughput methods to unravel the multiple targets of miRNAs.
3rd World Congress on Regenerative Medicine, ncRNA workshop, 2007 October 18 - 20, Leipzig

Schutt K, Michel M, Ullmann K, Schulz C, Stadler PF, Mörl M, Horn F, Hackermüller J, Kretzschmar AK.
In vivo analysis of RNA-RNA interactions: Development of efficient high throughput methods to unravel the multiple targets of miRNAs.
6th Leipzig Research Festival for Life Sciences, 2007 December 13 - 14, Leipzig

Scutt N, Stolzing A, Scutt A.
The effect of in vivo ageing on rat tendon cells.
3rd World Congress on Regenerative Medicine, 2007 October 18 - 20, Leipzig

Stevens-Smith J, Stolzing A, Scutt A.
The effect of oxidative stress on bone formation in vivo.
3rd World Congress on Regenerative Medicine, 2007 October 18 - 20, Leipzig

Stolzing A, Grune T.
Degradation of oxidized proteins in aged microglial cells.
Tissue aging, 2007 September 28 - 30, Halle

Stolzing A, Sellars D, Scutt A.
Mesenchymal stem cells and bone fracture risk in diabetes mellitus.
3rd World Congress on Regenerative Medicine, 2007 October 18 - 20, Leipzig

Taube S, Stuttfeld E, zur Nieden NI.
Steering embryonic stem cell fate towards osteoblasts with downstream non-canonical wnt targets in vitro.
3rd World Congress on Regenerative Medicine, 2007 October 18 - 20, Leipzig

Taube S, zur Nieden NI.
Steering embryonic stem cell fate towards osteoblasts with downstream non-canonical wnt targets in vitro.
2nd GSSCR, 2007 October 4 - 6, Würzburg

Thomas J, Mögling R, Breun SKJ, Baumann JG.
Tailor-made retroviral vector systems for applications in cell biology, virology, and immunology.
6th Leipzig Research Festival for Life Sciences, 2007 December 13 - 14, Leipzig

Trepke S, Breun SKJ, Baumann JG.
Retroviral vector design for stable cell transduction.
3rd World Congress on Regenerative Medicine, 2007 October 18 - 20, Leipzig

Trettner S, Fleischmann G, Horn PA, Sasaki E, zur Nieden NI.
Osteogenesis in marmoset embryonic stem cells.
3rd World Congress on Regenerative Medicine, 2007 October 18 - 20, Leipzig

Trettner S, Kuske B, Rancourt DE, zur Nieden NI.
In vitro osteogenesis of embryonic stem cells – an interspecies comparison.
2nd Abcam Stem Cell Symposium, 2007 December 13 - 16, Punta Cana, Dominican Republic

Trettner S, Sasaki E, zur Nieden NI.
3-D bioprocess development for osteogenic differentiation of marmoset embryonic stem cells.
Saxon Biotechnology Symposium, 2007 November 28, Dresden

Trettner S, Taube S, Sasaki E, zur Nieden NI.
Feeder-free culture and in vitro osteogenesis of marmoset ESCs.
Canadian Stem Cell Network, 6th Annual General Meeting, 2007 November 7 - 9, Toronto, Canada

Trettner S, Sasaki E, zur Nieden NI.
Development of an automated 3-D bioprocess for osteogenic differentiation of primate embryonic stem cells.
6th Leipzig Research Festival for Life Sciences, 2007 December 13 - 14, Leipzig

Ullmann K, Kretzschmar AK, Hackermüller J, Schreiber S, Schulz C, Stadler PF, Horn F.
Identification, validation and characterization of novel prostate cancer specific microRNAs.
3rd World Congress on Regenerative Medicine, ncRNA workshop, 2007 October 18 - 20, Leipzig

Ullmann K, Kretzschmar AK, Hackermüller J, Schreiber S, Schulz C, Stadler PF, Horn F.
Identification, validation and characterization of novel prostate cancer specific microRNAs.
6th Leipzig Research Festival for Life Sciences, 2007 December 13 - 14, Leipzig

Wagner DC, Schmidt UR, Förschler A, Kamprad M, Schwarz S, Egger D, Emmrich F, Boltze, J.
In vivo infarct volumetric analysis upon experimental stroke in rat using a 1.5T clinic MR scanner – an investigation of lesion development comparing local versus systemic stem cell administration.
3rd World Congress on Regenerative Medicine, 2007 October 18 - 20, Leipzig

Wagner DC, Schmidt UR, Förschler A, Kamprad M, Schwarz S, Emmrich F, Boltze J.
Intravenous versus intrastriatal transplantation of human fetal midbrain neural stem cells upon experimental stroke – a comparison of lesion development and sensomotoric benefits.
NeuroScience Conference, 2007 November 3-7, San Diego, USA

Wegehaupt A, Breun SKJ, KewalRamani VN, Baumann JG.
Library screens for the identification of therapeutic targets.
3rd World Congress on Regenerative Medicine, 2007 October 18 - 20, Leipzig

Wilcke A, Weißfuß J, Kirsten H, Ahnert P.
Genetic basics of dyslexia.
IBIDA, 21nd Annual Conference, 2007 October 11-12, Oakbrook Terrace, USA

Wilcke A.
Genetische Grundlagen der Legasthenie.
Second All-European Dyslexia Conference, 2007 November 15 - 17, Luxemburg, Luxemburg

zur Nieden NI, Davis LA, Price FD, Geransar RM, Stuttfeld E, Taube S, Kuske B, Rancourt DE.
Cell Fate Decisions of Embryonic Stem Cells Are Controlled by Soluble Factors and Physical Cues.
Seminar series, Donau-University Krems, 2007 October 13, Krems, Austria

zur Nieden NI, Davis LA, Price FD, Geransar RM, Stuttfeld E, Taube S, Kuske B, Rancourt DE.
Underlying molecular regulations of fate decisions in embryonic stem cells: beta-catenin and co-activators.
3rd International Workshop on Concepts and Mathematical Models of Stem Cell Organization, 2007 September 24 - 26, Machern

zur Nieden NI, Davis LA, Rancourt DE.
Novel endpoints to assess developmental osteotoxicity in the embryonic stem cell model.
48th International Meeting of the German Society of Pharmacology and Toxicology (DGPT), 2007 March 5 - 7, Mainz

zur Nieden NI.
Manipulating Wnt signals to steer osteogenic fate in embryonic stem cells.
Mini Symposium "Stem Cells for Skeletal Regeneration", 2007 May 20, Calgary, Canada

zur Nieden NI.
Markers of differentiation as endpoints for assessment.
HESI Workshop on Alternative Assays for Developmental Toxicity, 2007 February 27 - 28, Cary, NC, USA

zur Nieden NI.
Non-canonical wnt signaling modulates proliferation and expression of early osteoblast markers during osteogenic commitment. A40, 2007 February.
BMBF BioFUTURE, 2007 January 28 - 29, Berlin

zur Nieden NI.
Primate embryonic stem cells.
2nd Fraunhofer Life Science Symposium, 2007 October 17, Leipzig

Prizes

Boltze J.
Forschungspreis: Zelltherapie des Schlaganfalls.
THERACUR Stiftung

Fricke S.
Posterpreis: GvHD Modell in triple transgenen Mäusen.
Deutsche Gesellschaft für Immunologie

zur Nieden NI.
Alumni Award: Bester ehemaliger Trainee des Netzwerkes (Auszeichnung für Leistungen in der Optimierung von Stammzelldifferenzierungsprozessen).
Canadian Stem Cell Network

zur Nieden NI.
IQ Innovationspreis Mitteldeutschland, Top 10 Finalist: Erweiterung eines in vitro Embryotoxizitätstests

zur Nieden NI.
Nominierter und ausgewählter Teilnehmer des Nobellaureaten Treffens: Herausragende Leistungen für die entsprechende Karrierestufe, Auszeichnung für allgemeine Leistung in der Wissenschaft.
Fraunhofer-Gesellschaft

Dissertations

Feik, Sandra.
Entwicklung einer Methode zur Untersuchung von RNA-Protein-Interaktionen in Zellkultur.
Diplomarbeit, Universität Leipzig

Fricke, Stephan.
Molekularbiologische Diagnostik invasiver Aspergillosen mittels LightCycler-PCR-Technik.
Promotion, Universität Leipzig

Michel, Marcus.
Etablierung einer Methode zum Nachweis von RNA-RNA-Interaktionen und micro-RNA-Zielgenen.
Diplomarbeit, Universität Leipzig

Wilcke, Arndt.
Genetische Grundlagen der Legasthenie.
Diplomarbeit, Universität Leipzig

Wolf, Doris.
Charakterisierung und Phänotypisierung der murinen Stammzelllinie MuSC-E8.
Diplomarbeit, Universität Leipzig

Introducing the Fraunhofer-Gesellschaft

Aims and Principles

The Fraunhofer-Gesellschaft is one of Germany's big four research organizations. It is currently the largest European organization conducting applied research, the outcome of which has direct benefits for business and society. Its clients and contract partners include industrial companies, the service sector and the public sector. By developing state-of-the-art technology on behalf of its clients, the various Fraunhofer institutes help reinforce the competitive strength of the economy in their local region as well as throughout Germany and Europe. Ultimately, the Fraunhofer-Gesellschaft aims to promote the development of a society that is economically successful without losing sight of social welfare or environmental responsibility. The Fraunhofer-Gesellschaft was founded in 1949 and is a recognized nonprofit organization. Its members include prestigious companies and private patrons, who help shape Fraunhofer's research policy and strategic development. The organization was named after Joseph von Fraunhofer (1787–1826), an optician from Munich, who became a successful researcher, inventor and entrepreneur.

Structure

The Fraunhofer-Gesellschaft maintains 56 institutes with around 80 research units at more than 40 locations in Germany. The vast majority of the nearly 13,000 staff are qualified scientists and engineers. They work with an annual research budget of more than 1.2 billion euros, over 900 million euros of which is generated through contract research. Roughly two thirds of the Fraunhofer-Gesellschaft's research revenue stems from industry contracts and publicly financed research. The remainder is contributed by national and regional governments, partly as a means of enabling the institutes to pursue fundamental research in areas that are first likely to become relevant to industry and society after five or ten years. Affiliated research centers and branches in Europe, the USA and Asia facilitate contact to the main regions of current and future scientific progress and economic development. As an employer, the Fraunhofer-Gesellschaft offers its staff the opportunity to develop the professional and personal skills they need to take up positions of responsibility within their institute, in other scientific domains and in business and society.

Alliances in the Fraunhofer-Gesellschaft

The Fraunhofer-Gesellschaft is divided into seven thematic groups with separate offices to coordinate their joint activities.

- information and communication technology
- microelectronics
- production
- materials and components
- life sciences
- surface technology and photonics
- defense and security

Fraunhofer Life Sciences Alliance

To strengthen the biosciences, biomedicine and biotechnology, in 2001 the Fraunhofer Life Sciences Alliance was created, it comprises Fraunhofer IBMT, Fraunhofer IGB, Fraunhofer IME, Fraunhofer ITEM, Fraunhofer IZI, and the in 2007 established Fraunhofer IVV.

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

As far as its future development is concerned, the Fraunhofer Life Sciences Alliance focuses on four core competencies harboring excellent business prospects.

The elected spokesman of the Fraunhofer Life Sciences Alliance is Prof. Uwe Heinrich, who heads the Fraunhofer Institute for Toxicology and Experimental Medicine (Fraunhofer ITEM) in Hanover.

Fraunhofer IZI has always been a member of the Fraunhofer Life Sciences Alliance, and judging by the market experience of the various life sciences institutes, it appears unlikely that the Fraunhofer-Gesellschaft will ever be able to finance long-term, risky pharmaceutical product development under its own auspices. Therefore, the institutes in the Fraunhofer Life Sciences Alliance (including Fraunhofer IZI) concentrate on developing and offering research-intensive services. However, this does not rule out the possibility of internally financed developments being taken to an advanced level on occasion – especially in the field of new cell and tissue engineering products.

Core Competencies of the Fraunhofer Life Sciences Alliance

- accelerated drug development
- regenerative medicine
- production and safety of foods and animal feed
- biotechnical production, evaluation

Institutes in the Fraunhofer Life Sciences Alliance

Fraunhofer Institute for Biomedical Engineering (IBMT)
Ensheimer Straße 48
66386 St. Ingbert
Phone: +49 (0) 6894/980-0
www.ibtm.fraunhofer.de
info@ibmt.fraunhofer.de

Fraunhofer Institute for Interfacial Engineering and Biotechnology (IGB)
Nobelstraße 12
70569 Stuttgart
Phone: +49 (0) 711/970-4001
www.igb.fraunhofer.de
info@igb.fraunhofer.de

Fraunhofer Institute for Molecular Biology and Applied Ecology (IME)
Forckenbeckstraße 6
52074 Aachen
Phone: +49 (0) 241/60 85-0
www.ime.fraunhofer.de
info@ime.fraunhofer.de

Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM)
Nikolai-Fuchs-Straße 1
Haupteingang: Stadtfelddamm
30625 Hannover
Phone: +49 (0) 511/53 50-0
www.item.fraunhofer.de
sekretariat@item.fraunhofer.de

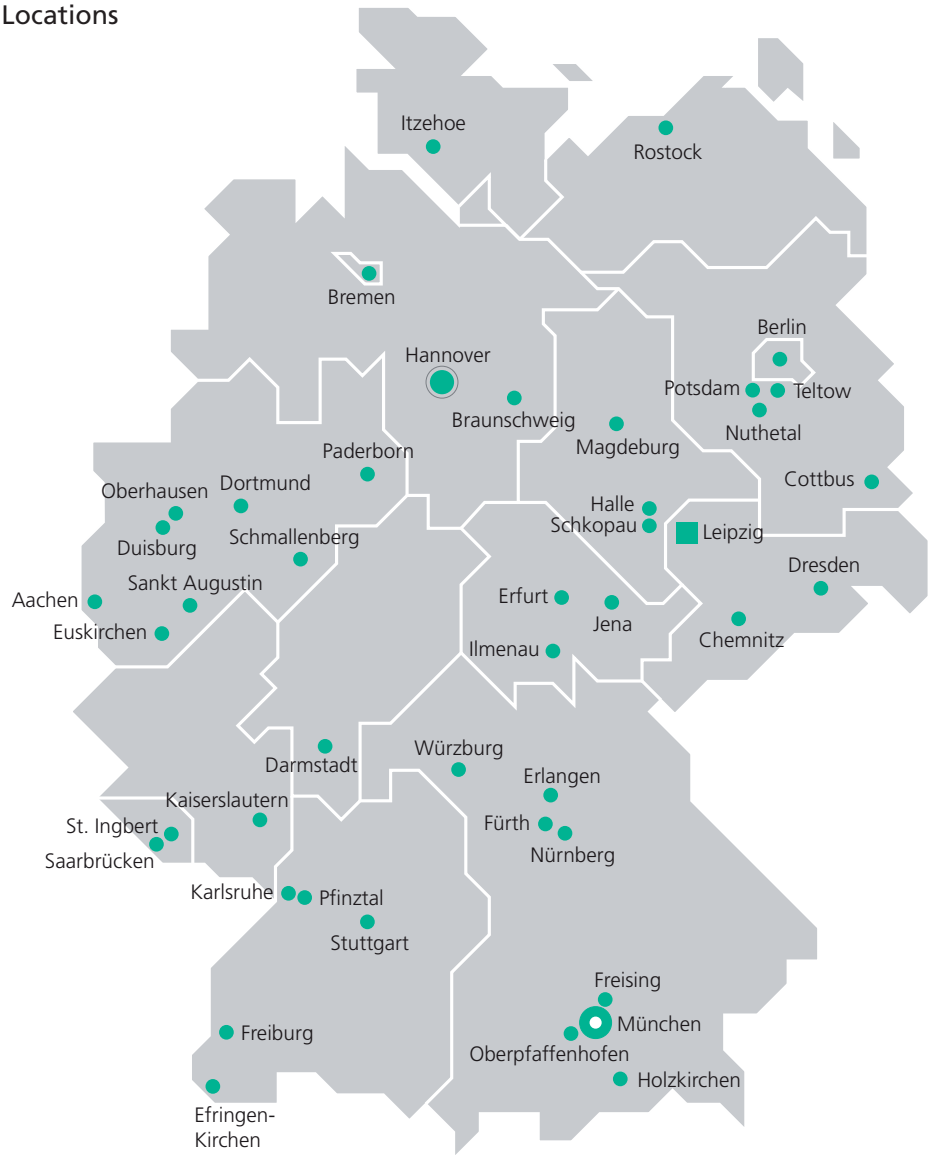
Fraunhofer Institute for Cell Therapy and Immunology (IZI)
Perlickstraße 1
04103 Leipzig
Phone: +49 (0) 341/355 36-1000
www.izi.fraunhofer.de
info@izi.fraunhofer.de

Fraunhofer Institute for Process Engineering and Packaging (IVV)
Giggenhauser Straße 35
85354 Freising
Phone: +49 (0) 8161/491-0
www.ivv.fraunhofer.de
info@ivv.fraunhofer.de

Head of the Fraunhofer Life Sciences Alliance

Dr. Claus-Dieter Kroggel
Fraunhofer Institute for Toxicology and Experimental Medicine
Nikolai-Fuchs-Str. 1
30625 Hannover
Phone: +49 (0) 511/53 50-103
www.lifesciences.fraunhofer.de
claus.kroggel@vls.fraunhofer.de

Locations



Central Office, Munich

Central Office of the Fraunhofer Life Sciences Alliance, Hanover

Fraunhofer IZI, Leipzig

Head Office

Fraunhofer-Gesellschaft zur Förderung der angewandten Forschung e. V.
Hansastrasse 27c
80686 München
Phone: +49 (0) 89/12 05-0
Fax: +49 (0) 89/12 05-7531
info@fraunhofer.de
www.fraunhofer.de

Executive Board:
Prof. Dr. Hans-Jörg Bullinger,
President of the Fraunhofer-Gesellschaft, Corporate Management and Research

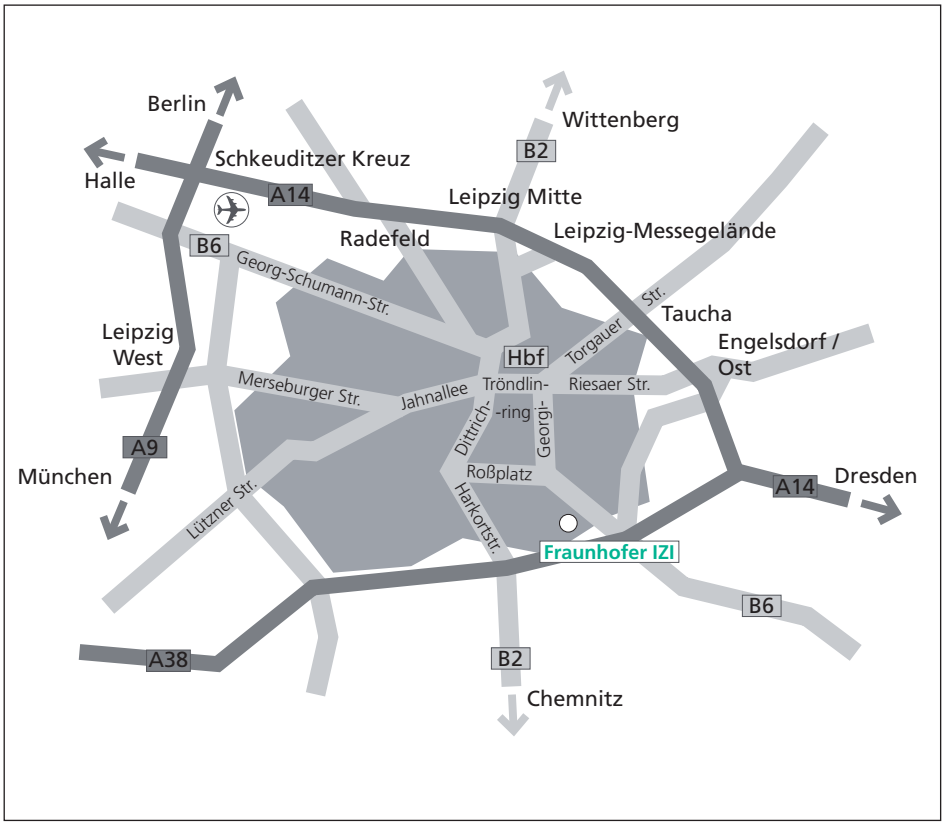
Prof. Dr. Ulrich Buller,
Research Planning

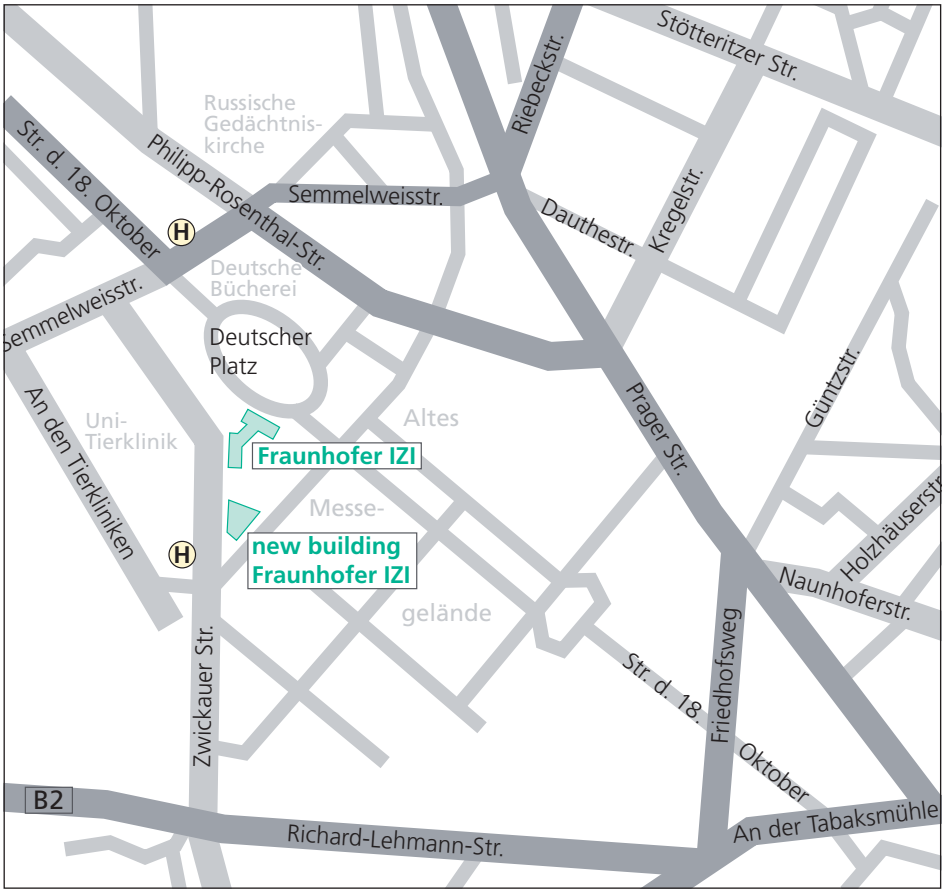
Dr. Alfred Gossner,
Finance and Controlling (including Business Management, Purchasing, Real Estate), IT

Press and PR:
Franz Miller
Phone: +49 (0) 89/12 05-1300
Fax: +49 (0) 89/12 05-7513
franz.miller@zv.fraunhofer.de

Historical Fraunhofer Glasworks
Fraunhoferstrasse 1
83671 Benediktbeuern

Function	Contact	Phone / Email
Equal Opportunities, Procurement, Controlling	Annette Schäfer	Phone: +49 (0) 341 / 355 36-9220 annette.schaefer@izi.fraunhofer.de
Biological and General Safety	Dr. Andreas Schubert	Phone: +49 (0) 341 / 355 36-5105 andreas.schubert@izi.fraunhofer.de
Operation Engineer	Falk Hoffmann	Phone: +49 (0) 341 / 355 36-9555 falk.hoffmann@izi.fraunhofer.de
Project Service, Business Development, PR	Dr. Wilhelm Gerdes	Phone: +49 (0) 341 / 355 36-9300 wilhem.gerdes@izi.fraunhofer.de
GMP Officer, Head of Production (Drugs Act)	Dr. Gerno Schmiedeknecht	Phone: +49 (0) 341 / 355 36-9705 gerno.schmiedeknecht@izi.fraunhofer.de
Equipment Management, Safety	Dirk Peisker	Phone: +49 (0) 341 / 355 36-9533 dirk.peisker@izi.fraunhofer.de
Head of Institute	Prof. Dr. Frank Emmrich	Phone: +49 (0) 341 / 355 36-9105 frank.emmrich@izi.fraunhofer.de
IT-Manager	Raik Pechfelder	Phone: +49 (0) 341 / 355 36-9610 raik.pechfelder@izi.fraunhofer.de
Head of GLP test facility, responibility under Section 47(2) Infection Protection Act	Dr. Jörg Lehmann	Phone: +49 (0) 341 / 355 36-1205 joerg.lehmann@izi.fraunhofer.de
Head of Quality Control	Prof. Dr. Ulrich Sack	Phone: +49 (0) 341 / 97 25-506 ulrich.sack@izi.fraunhofer.de
Project Management under Section 3(8) Genetic Engineering Act	Dr. Sebastian Ulbert	Phone: +49 (0) 341 / 355 36-2106 sebastian.ulbert@izi.fraunhofer.de
GMP Quality Assurance, Responsible Person under Drugs Act	Catharina Frey-Duisberg	Phone: +49 (0) 341 / 355 36-9710 catharina.frey-duisberg@izi.fraunhofer.de
Responsibility under Section 47(2) Infection Protection Act	Dr. Jens Knauer	Phone: +49 (0) 341 / 355 36-1206 jens.knauer@izi.fraunhofer.de
Administration, Intellectual Property Rights, Personnel Development	Patric Nitz	Phone: +49 (0) 341 / 355 36-9200 patric.nitz@izi.fraunhofer.de





Fraunhofer Institute for Cell Therapy and Immunology
Perlickstraße 1
04103 Leipzig

How to Reach Us

By Car

A9 Exit the motorway at "Leipzig-West". Take the B181 in the direction of "Zentrum." Follow the B87 (Merseburger Strasse, Lützner Strasse, Jahnallee), after the central railway station, turn right towards "Augustusplatz" (Leipzig Opera House), then take Prager Strasse, turn off towards "Alte Messe."

A14 Exit the motorway at "Leipzig-Mitte". Take the B2 (via Maximilianallee) heading for the city center (Zentrum). Follow the B2 (via Gerichtsweg and Prager Strasse), exit from Prager Strasse towards "Alte Messe."

A38 Exit the motorway at "Leipzig-Süd". Take the B2 heading towards "Leipzig Zentrum". Turn off into Richard-Lehmann-Strasse. Follow Richard-Lehmann-Strasse and exit at (before) the BMW car show room towards "Alte Messe".

Public Transport

Travel to the Leipzig "Hauptbahnhof" (central railway station), take the no. 16 tram heading for "Lössnig". Alight at the "Deutsche Bücherei" (German National Library and the main entrance to the BIO CITY) or "An den Tierkliniken" (rear entrance to the BIO CITY).

From the Airport

Take the train to Leipzig "Hauptbahnhof" (central railway station), then continue by tram (see above).

We will gladly send you further information regarding our Institute, current projects, co-operation possibilities and service offerings. Starting from May 2008 our comprehensive service catalog will be electronically available as an online brochure.

You may tear off an insert below, complete the requested information and return it to us and we will mail you an information package .
Thank you.

Alternatively, send a fax to:
+49 (0) 341/355 36-9921

or an email to:
info@izi.fraunhofer.de

Sender
Name: .....
Company/Institute: .....
Address: .....
.....
Email: .....

Fraunhofer-Institut
für Zelltherapie und Immunologie
Öffentlichkeitsarbeit
Perlickstraße 1
04103 Leipzig

www.izi.fraunhofer.de
info@izi.fraunhofer.de
Fax: +49 (0) 341/355 36-9921

Please send me the following information:
☐ Fraunhofer IZI service catalog
☐ Annual Report 2007
☐ current Fraunhofer IZI project information
☐ information on the Fraunhofer Life Sciences Alliance
☐ information on:
.....
.....
.....
.....

Sender
Name: .....
Company/Institute: .....
Address: .....
.....
Email: .....

Fraunhofer-Institut
für Zelltherapie und Immunologie
Öffentlichkeitsarbeit
Perlickstraße 1
04103 Leipzig

www.izi.fraunhofer.de
info@izi.fraunhofer.de
Fax: +49 (0) 341/355 36-9921

Please send me the following information:
☐ Fraunhofer IZI service catalog
☐ Annual Report 2007
☐ current Fraunhofer IZI project information
☐ information on the Fraunhofer Life Sciences Alliance
☐ information on:
.....
.....
.....
.....

Editorial Team
Frank Emmrich
Wilhelm Gerdes
Jens Augustin
Christina Kühn

Devised by
Frank Emmrich
Wilhelm Gerdes
Jens Augustin
Christina Kühn

Layout & Typesetting
Michaela Grahn

Translation
Audrey Braun
Dr. Jan Matthias Braun

Picture Credits
Titelbild: Tina Kopetzky – student at Geschwister Scholl Grammar School Taucha, awarded in the student competition on regenerative medicine on the occasion of the World Congress 2007 in Leipzig.

Fotostudio Schokoauge, Leipzig

Margit Emmrich

all other pictures and figures:
Fraunhofer IZI

Printed by
DZA Druckerei zu Altenburg GmbH, Altenburg

Editorial Address
Fraunhofer-Institut für Zelltherapie und Immunologie
Perlickstraße 1
04103 Leipzig
Germany

www.izi.fraunhofer.de
wilhelm.gerdes@izi.fraunhofer.de

Fraunhofer Institute for Cell Therapy and Immunology
Perlickstraße 1
04103 Leipzig
Germany

Phone: +49 (0) 341/355 36-1000
Fax: +49 (0) 341/355 36-9921
www.izi.fraunhofer.de
info@izi.fraunhofer.de