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Biomedical Research at the Johannes Gutenberg University Medical Center has seen an exceptional development in the last few years. The University Medical Center has been striving to translate the understanding of basic biological processes into high impact clinical applications. In the year 2013 – as in the years before – the University Medical Center maintained a research environment that cultivates the best minds in biomedical science and medicine and attracts talented new individuals to our faculty and staff. We realize that enormous opportunities exist for advancing our understanding of basic biological processes with the long-term goal of improving the health of our patients. Let me point out a few highlights of the year 2013.

At first, I would like to draw your attention to the Paul-Klein-Center for Immune Intervention (PKZ). This building is currently under construction at the south-west corner of our Medical campus. The total cost of € 34 million is financed jointly by the Federal Government and the State of Rhineland-Palatinate according to Art. 91b of the Federal Constitution. Once completed, the PKZ will be home to most of our research groups in the field of immunology and immunotherapy, working under the umbrella of the Research center for immunotherapy (FZI). Immunology – with all its facets – has been a scientific stronghold of the University Medical center for decades. In 2013, a new Collaborative Research Center (SFB 1066) “nanodimensional polymer therapeutics for tumor therapy” (applied for together with the Faculty for chemistry of the University) commenced its work in this area of research.

Another ongoing construction project of € 42 million, also financed according to Art. 91b of the Federal Constitution, is the Biomedical Research Center on the campus of the Johannes Gutenberg University. Researchers of the Focus program translational neuroscience (FTN) submitted the proposal that was approved by the German Science Council. One focus of the FTN are studies of the molecular and cellular interactions that allow the brain to maintain a state of equilibrium or homeostasis, which is the basis of resilience against external stressors. Together with colleagues in Frankfurt, members of FTN successfully started a new Collaborative Research Center in 2013 (SFB 1080) on this topic: “Molecular and cellular mechanisms of neural homeostasis”.

A second focus of FTN is neuroimmunology, which links this program to the FZI immunology program.

The third research stronghold of the University Medical Center is vascular biology. The Center for Translational Vascular Biology (CTVB) was instrumental in attracting funds for an Integrated Research and Treatment Center from the Federal Ministry for Education and Research. This "Center for Thrombosis and Hemostasis (CTH)" has largely expanded our proficiency in this area and is highly complementary to our vascular biology expertise. In 2013, we appointed Wolfram Ruf into this research consortium as the first Professor of the Humboldt Foundation at the University Medical Center.

The University Medical center realizes that funding opportunities shift increasingly to the European level. To name only one European accomplishment, the European Commission started the funding of nine research projects of the University Medical Center. For two of those projects, PanCareLife and Neurokine, the overall coordination lies in the hands of the University Medical Center. Together, these European projects have a budget of more than € 1.5 million. PanCareLife will focus on the late effects of childhood tumor therapy, such as fertility problems and hearing loss. The core objective of the Neurokine research network is to gain insight into the impairment of communication between immune cells.

2013 was a successful, but also a demanding year for the University Medical center. The event "Quo Vadis University Medical center" (in August 2013) demonstrated that the University Medical center has a well defined research strategy, which, nevertheless, needs to be adapted and improved continuously.

Finally, I would like to thank all colleagues and cooperation partners for their dedication and continuous support. Together we create a center of excellence in research to the benefit of our patients.

From summarized research activities to overviews about our individual departments and colleagues, the current research report will provide you with all relevant information about the University Medical Center Mainz in 2013.

With best regards,

Ulrich Förstermann
Mainz, December 2014
Funding of Open Access

On January 25, the Johannes Gutenberg University joined the Berlin Declaration on Open Access to Knowledge in the Sciences and Humanities. Scientists of Johannes Gutenberg University and University Medical Center are permitted to request resources of the publication fund 2013 that contains € 85,000.

Handing-over of duties to new Chief Scientific Officer

Starting April 1, Professor Ulrich Förstermann is the new Chief Scientific Officer (CSO) and Dean of the University Medical Center. He supersedes Professor Reinhard Urban, whose time as CSO started in 2001 and lasted six terms until March 31, 2013.

Professor Wolfram Ruf accedes Humboldt-chair at University Medical Center

On April 1, elite researcher Professor Wolfram Ruf ends his work in the USA and starts working at University Medical Center. He is considered an internationally acknowledged expert in sector of blood clotting.

Launch of the Chinese-German Center for Bio-Inspired Materials at the University Medical Center

A German research team has launched a Chinese-German Joint Center for Bio-Inspired Materials. It is led by Professor Werner E. G. Müller of the Institute of Physiological Chemistry at the University Medical Center as well as scientists from the Chinese Academy of Sciences and the Chinese Academy of Geological Sciences. The aim is to use the strategy of marine animals to develop novel bio-inspired bone replacement materials and medications to ameliorate osteoporosis.

Edith Heischkel Mentoring Program helps women with their careers

The Edith Heischkel Mentoring Program aims to gain young scientists in leading positions and thereby help the University Medical Center become sustainable. The program exists since 2008 and in this year’s sixth round 13 young scientists will be mentored by experienced scientists for one year.

German Science Council recommends funding of neurosciences research building at the Mainz University Medical Center

The German Science Council has recommended federal and state funding for a neurosciences research building at the Mainz University Medical Center. The central aim of the funding program is to finance the construction of buildings for scientific projects with national significance that are characterized by innovative and interdisciplinary research approaches. This decision indicates strong recognition of the researchers of the Focus Program Translational Neuroscience (FTN) at Johannes Gutenberg University Mainz who submitted the proposal.
MILESTONES 2013

Breakthrough discovery: Improved mass spectrometric method for proteomic analyses

Mass spectrometry is a highly sensitive method of measurement that is used to analyze cell components, body fluids or developing new medications. Professor Stefan Tenzer of the Institute of Immunology and his colleagues have now significantly improved this analytical method. It is a data-independent technique that facilitates a very accurate and reproducible quantitative analysis. Moreover, they have developed a software program for the integrated analysis of measurement data called ISOQuant.

German Research Foundation approves establishment of new Research Training Group „Life Sciences, Life Writing“

An interdisciplinary group will examine how new biomedical capabilities can lead to extreme experiences in human life. Specifically, it deals with issues arising from the technologically assisted reproduction or medically assisted death. The Research Training Group „Life Sciences, Life Writing: Extreme Experience in Human Life between Biomedical Explanations and Worldly Experience“ offers 12 doctoral candidates a structured research and training program, starting April 2014. The German Research Foundation will initially provide approximately € 7 million to the research unit for four and a half years.

Publication of the Women’s Promotional Plan 2013-2019

For the first time since the fusion of the University Clinic with the Johannes Gutenberg University Mainz School of Medicine, a combined Women’s Promotional Plan for non-scientific and scientific employment was published in December. The goal of the entire Women’s Promotional Program is to guarantee occupational equality for men and women.

Boehringer Ingelheim supports Gutenberg Health Study for four more years

With € 3 million Boehringer Ingelheim continues funding of the Gutenberg Health Study, a large-scale prospective and population-based study. The aim is to construct a bio databank on the basis of the gathered bio information.

Boehringer Ingelheim Prize 2013

The molecular scientist Dr. Nir Yogev (l.) and the psychologist Dr. Iris Reiner (r.) share the Boehringer Ingelheim Prize 2013. The prize is remunerated with € 30,000 and was handed over solemnly on July 3.

University Medical Center presents inventions at PharmaForum

Several scientists of the University Medical Center Mainz presented their medical inventions with high innovative potential at the 2013 PharmaForum, hosted by ZDF headquarters in Mainz.

Visit at Hebrew University of Jerusalem

From October 21 to 23, Professor Ulrich Förstermann together with a delegation of the University Medical Center visited the Hebrew University of Jerusalem, one of the world’s elite universities. The aim of the visit was to look at mutual interests and opportunities for cooperation.

New collaborative research center “Nanodimensional polymer therapeutics for tumor therapy”

The opening ceremony on October 22 was the beginning of the collaborative research center “Nanodimensional polymer therapeutics for tumor therapy,” (SFB 1066), which is jointly constructed with the University Medical Center and the Max-Planck Institute for Polymer Research. The German Research Foundation supports the new research center with approximately € 11 million over the next four years. Based on nanoparticles, a tumor-model should be developed for a new tumor therapy against Melanoma.

European Commission supports new research network

The European Commission is providing € 6 million for a European research project named “ncRNAPain” (Non-coding RNAs in a neurogenic and neuropathic pain mechanisms and their application for risk assessment, patient stratification and personalised pain medicine). The research project aims to identify specific ncRNAs. On behalf of the University Medical Center, the project group of Professor Frank Birklein is actively involved.
Research Activities

The following charts present the key performance indicators for research activities of the University Medical Center Mainz. An overview like this allows an in-depth analysis of the national and international standing of a University Medical Center. The numbers can be divided in four categories. Those are: funding, publications, technology transfer and promotion of young researchers.

I. FUNDING

Figure 1 shows the third-party funding expenditures from 2009 to 2013. In 2013 those funding expenditures increased by 18.4% compared to 2012 and amounted more than € 54 million. 2013's third-party funding expenditures make an all-time high of the University Medical Center Mainz. This development is mainly attributable to a rise in funding for the medical units conservative medicine and general medicine.

The different medical units of the University Medical Center Mainz had different amounts of third-party funding, since ever. Those differences result from the unequal conditions in number of funding programs for the different units as well as diverging effort spent on funding applications.

The significant rise in third-party funding expenditures enables researchers at University Medical Center Mainz to invest more in their scientific projects and enlarge the number of publications.

Industrial projects (29%), the German Research Foundation (23%) and federal projects (19%) are the largest founding sources. The great stake of industrial funding shows that the research projects at University Medical Center Mainz are highly relevant for practitioners.

II. PUBLICATIONS

Not only the third-party funding expenditure, but also the number of publications with impact factor points rose to an all-time high of 1095 in 2013 (Figure 3). This development is closely linked to the higher amount of funding, as promising scientific projects more or less directly lead to a higher number of publications.

The large amount of publications strengthens the national and international standing of the University Medical Center Mainz.
Figure 4 shows that the sum of impact factors for all publications in 2013 increased by 14% compared to previous year.

Person-related cumulative impact factors (CiF) have been used to evaluate the overall performance of scientists within an institute. In doing this, the impact factor points from all publications (1605 CiF-points in 2013) were compiled for each area. The calculation was based on the German Council of Science and Humanities’ guidelines. The cumulative impact factors are determined on an institute-by-institute basis and these in turn are the basis for internal performance-based fund allocation (PBFA).

In 2013, the number of staff with publications remained relatively the same compared to previous year (figure 5). The only bigger changes are noticeable in the medical units “Surgery” and “Departments of Dental Medicine”.

Figure 6 shows the number of staff with publications. Compared to 2012 this number decreased slightly from all in all 1150 to 1130 persons in 2013. This still large number proves that the scientists are highly motivated and ambitious about their research although the workload in many of the departments is enormous.

Figure 7 shows the top scientists who achieved a cumulative impact factor of more than 15.
While the key performance indicators in the category publications show the scientific standing of the University Medical Center Mainz, the category technology transfer rather focuses on the transferability of projects to medical practice.

Figure 8 shows the development of disclosed inventions. With 25 inventions in 2013 the number decreased by 19% compared to previous year. This fluctuation was quite expectable as the elaboration of an invention disclosure is comprehensive and as 2012 was a record high.

As a result of previous year’s high number of inventions and the promising character of disclosed inventions, the number of patent registrations increased significantly in 2013 (Figure 9). This rise is crucial, because firstly it endorses the reputation of the University Medical Center Mainz and secondly it generates income for the University Medical Center via sources such as long-term license fees on a long-term.

After the initial patent application which establishes priority (usually for the EU states), patent protection is often extended to new regions via additional patent applications in countries such as the United States and Japan. These additional applications are not included in the figures presented here.

The University Medical Center Mainz places strong emphasis on fostering and developing young research talent. One way to measure the success of young researchers is to take a look on the awards bestowed upon them. Once again, the number of doctorates awarded was upheld. In 2013, 310 doctorates were conferred at the University Medical Center. Human medicine received 238 awards and 68 went to dentistry. Three outstanding candidates received the title "summa cum laude". 24 scientists successfully completed their postdoctoral lecturing.

Although those numbers are already quite satisfying, it is targeted to reach the outstanding promotion results of the years 2010 and 2011 again.

The Postdoc Community proves the engagement and ambition of the University Medical Center’s young scientists, as it aims to create a network of scientific and social interactions among postdocs. In 2013, events like "Science needs Project Management" or "Ethics Proposal Preparation" provided useful interdisciplinary information for the postdocs. The Community was founded in 2010.
New Faculties 2013

Professor Markus Christmann  
Department of Toxicology  
University Medical Center of the Johannes Gutenberg-University Mainz  
Full Professorship (W2) for Research on DNA-Repair

Professor Björn E. Clausen  
Institute of Molecular Medicine  
Erasmus University Rotterdam  
Full Professorship (W2) for Experimental Molecular Medicine

Professor Andreas Diefenbach  
Institute of Medical Microbiology and Hygiene  
Albert-Ludwigs-University Freiburg  
Full Professorship (W3) for Medical Microbiology

Professor Stephan Gehring  
Center for Childhood and Adolescent Medicine (ZKM)  
University Medical Center of the Johannes Gutenberg-University Mainz  
Full Professorship (W2) for Specialized Pediatric Hepatology, Gastroenterology and Pediatric Intensive Care

Professor Julia B. Hennermann  
Center for Childhood and Adolescent Medicine (ZKM)  
Charité-University Medical Center Berlin  
Foundation professorship (W2) for metabolic storage diseases

Junior Professor Sven Kantelhard  
Department of Neurosurgery  
University Medical Center of the Johannes Gutenberg-University Mainz  
Junior Professorship for Intraoperative Imaging and Tissue Analysis

Professor Oliver Krämer  
Department of Toxicology  
Friedrich-Schiller-University Jena  
Full Professorship (W2) for Molecular Toxicology

Professor Thomas J. Musholt  
Department of General-, Abdominal and Transplantation Surgery  
University Medical Center of the Johannes Gutenberg-University Mainz  
Full Professorship (W2) (for life) for Endocrine Surgery

Professor Katrin Schäfer  
Department of Medicine 2 (Cardiology, Angiology and Intensive Care)  
Georg-August-University Göttingen  
Full Professorship (W2) for Translational Vascular Biology

Professor Wolfram Ruf  
Integrated Research and Treatment Center: Center of Thrombosis and Hemostasis (IFB CTH)  
The Scripps Research Institute, La Jolla, CA  
Alexander von Humboldt-Professor

Professor Wolfgang Retz  
Department of Psychiatry und Psychotherapy  
Saarland University  
Full Professorship (W2) for Forensic Psychiatry

Professor Michael S. Urschitz  
Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI)  
Eberhard Karls University Tübingen  
Full Professorship (W2) for Pediatric Epidemiology
Special Awards 2013

Professor Rainer Spessert
Institute of Functional and Clinical Anatomy
Teaching award 2013 of the Johannes Gutenberg-University of Mainz

Dr. Marlis Gerigk
Institute of Pathophysiology & Institute of Physiological Chemistry
Gerhard Theus Award 2013

Dr. Nina Hochhaus
Institute of Pathophysiology & Institute of Physiological Chemistry
Gerhard Theus Award 2013

Dr. Jens Uwe Marquardt
Department of Medicine I
Advancement Award GARPS 2013, Bad Kreuznach

PD Dr. Julia Menke
Department of Medicine I
Young Investigators Award, Sector Rheumatology, German Society of Internal Medicine

Dr. Jörn Fredrik Dopheide
Department of Medicine 2 (Cardiology, Angiology and Intensive Care)
UCB-Pharma-Award of the Society of Vascular Medicine 2013

Dr. Markus Bosmann
Department of Hematology, Pneumology and Oncology
Abstract Achievement Award (poster prize awarded by the American Society of Hematology) for a poster presentation on "Neuroendocrine regulation of the IL-27-dependent immune response in macrophages"

Patrick Derigs
Department of Hematology, Pneumology and Oncology
Doctoral fellowship granted by the German Cancer Aid

Dr. Helen Meyer-Martin
Department of Hematology, Pneumology and Oncology
Postgraduate award 2013 of the Deutsche Lungestiftung e.V. for the best experimental thesis in the field of pneumology "Evaluating a humanized mouse model of allergic respiratory tract inflammation"

PD Dr. Stephanie Korn
Department of Hematology, Pneumology and Oncology
Research award granted by the Südwestliche Gesellschaft für Pneumologie (highest award) for the work "Vitamin D insufficiency in severe and uncontrolled adult asthma and the EVITA trial"

PD Dr. Stephanie Korn
Department of Hematology, Pneumology and Oncology
Dagmar Ellner Award 2013 for the research work "Determination of free IgE levels in serum using a novel Recovery-ELISA in patients suffering from severe asthma and on treatment with Omalizumab"

Katharina Kukla
Department of Hematology, Pneumology and Oncology
CIIMT poster prize awarded at the 11th CIIMT (Association for Cancer Immunotherapy) symposium

Dr. Daniel Sasca
Department of Hematology, Pneumology and Oncology
Abstract Achievement Award (poster prize awarded by the American Society of Hematology) for a poster presentation on "Expression of FLT3-ITD dysregulates the DBC1-Sirt1-p53 signaling and promotes therapy resistance"

Professor Klaus Lieb
Department of Psychiatry and Psychotherapy
Hamburger Prize for Personality Disorders 2013

Dipl. Psych. Jutta Stoffers
Department of Psychiatry and Psychotherapy
Hamburger Prize for Personality Disorders 2013

Dr. Iris Reiner
Department of Psychosomatic Medicine
Boehringer Ingelheim Prize 2013

Professor Peter Brockерhoff
Department of Obstetrics and Gynecology
Appointment to honorary member of the German Society for Perinatal Medicine (DGPM) for his merits in the field of obstetrics

Dr. Constanze Bening
Department of Cardiology and Vascular Surgery
2013 Research Prize of the Support Group for the Dresden Cardiovascular Conference

Dr. Naureen Keric
Department of Neurosurgery
Foundation for Neurosurgical Research

PD Dr. Christian Thomas
Department of Urology
Maximilian Nitze Prize of the German Society of Urology 2013

Dr. Nir Yogev
Institute of Molecular Medicine
Boehringer Ingelheim Prize 2013

Janet Friedrich
Department of Diagnostic and Interventional Radiology
Young Investigator Award (DGMP)

Dr. Sebastian Schotten,
Dr. Daniel Pinto dos Santos
Department of Diagnostic and Interventional Radiology
Poster prize of the German Society of Interventional Radiology

Professor Wolfram Ruf
Integrated Research and Treatment Center: Center of Thrombosis and Hemostasis (IFB CTH)
Alexander von Humboldt-Chair

Dr. Markus Bosmann
Integrated Research and Treatment Center: Center of Thrombosis and Hemostasis (IFB CTH)
Award of the European Hematology Association (EHA)
Research Entities

- Key Research Center of Translational Medicine
- Key Research Area
- Research Cluster
- Profile Center
- Key Scientific Research Platforms
- Key Scientific Teaching Platform
In 2013 the Focus Program Translational Neuroscience (FTN) has continued to push its activities in appointing additional group leaders in strategic important positions. Apart from the 2011 established FTN platforms (MouseBehaviorUnitMBU and ProtocolsTranscriptomicsUnitProTic) and the already existing research platforms Animal Imaging Center (MAIC), Neuroimaging Center (NIF), the FTN enhanced its series of strategic appointments in 2013 with Prof. Marianne Müller-Sitz, Department of Psychiatry and Psychotherapy, and Jun.-Prof. Mai Stüttgen, Institute for Pathophysiology.

As an important milestone on the pathway to establish neuroscience research in Mainz as a center of national and international importance, funding for the reconstruction of the FTN-research building on University Campus and the coordination of the Neuroimaging Center was granted by the Wissenschaftsrat, with approximately 6000 m² of modern lab space including cutting-edge technology including 2-photon imaging, single cell MRI, and access to several technology platforms. These platforms, which include asthma core facility, confocal microscopy, immunohistochemistry, flow cytometry, conditional gene targeting as well as protein biochemistry and mass spectrometry, are available to researchers of the University Medical Center and the JGU.

In 2013 two new leading scientists could be recruited: Prof. Andreas Diefenbach (Head of the Institute for Medical Microbiology and Hygiene) and Prof. Björn E. Clausen (Experimental Molecular Medicine).

The research activities within the FTN will be centralized in the Paul Klein Center for Immunointervention (PKZ), which will be established through funding based on a research building application (according to Art.9b) until 2016. After the successful reviewing the CRC 1066 “Nanodimensional polymer therapeutics for tumor therapy” was initiated. In 2013 the FTN with Prof. Hansjörg Schild and Prof. Ari Waisman, The 43th Annual Meeting of the German Societies for Clinic research, was established.

The overall research theme of this platform varied the satellite projects enabled by the GBS is the explanation of molecular aspects of brain structure and function in neurodegenerative diseases (e.g., stress) in order to promote survival function and structural integrity, will be explained. The GBS closes an important gap in translational brain research. It is in the Department of Neurology and is led by PD Dr. med. Oliver Tüttcher.

In 2018 the Key Center was funded by the German Research Foundation (DFG) for 5 years (2018–2022) and the Mission of the Key Center is to create a platform linking basic research and bedside research.

The focus program translational neuroscience will continue its work in the coming years. Prof. Hansjörg Schild, Research director of the Key Center and spokesperson of the Key Center Translational Neuroscience in Mainz, said: "The key center will continue its work and will support the improvement of translational neuroscience in Mainz. Our focus will be on the development of new therapies and the implementation of these therapies into clinical practice."

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In 2013, the Center for Translational Vascular Biology (CTVB) focused on further sustaining and developing the key research projects which have been in the center of interest since the beginning: the Gutenberg Health Study (GHS), the German Center for Cardiovascular Research (DZHK) and the integrated research and treatment concept “Center of Thrombosis and Haemostasis (CTH)

The Gutenberg Health Study is one of the largest population-based cohort studies worldwide with a special focus on cardiac and vascular diseases. Investigations are predominantly based on multifactorial exposures, which potentially contribute to the development of cardiovascular disease, cancer, ophthalmological and metabolic disease, but also to disorders of the immune system and mental disease. The primary aim of the study is to improve a personalized risk prediction for these diseases. Therefore, cardiovascular risk factors, lifestyle, psychosocial, environmental and laboratory parameters as well as the extent of subclinical disease are taken into account.

A comprehensive biorepository enables molecular and genetic analyses, among others also in systems-oriented approaches. The results will help to develop new markers and targets for improving medical diagnostics, prognostics and therapy. In 2013, a comprehensive biomolecular analysis program was initiated (GHA Coagulation Panel, GHS Cardiovascular Biomarkers). Funding was acquired from various sources to extend the panel of biomarkers for the comprehensive investigation in a population-based, large-scale sample. The unique data set to assess the role of hemostasis for the development and progression of cardiovascular disease attracted the interest of further renowned researchers in the field (Prof. Hugo ten Cate and Dr. Henri Spronk, Biochemistry, CAIRM, Maastricht University).

Further academic and industrial funding was acquired to support the fast growing research portfolio of the CTVB and the institutions’ structures involved (e.g. a DFG grant for the research project “Cardiac and vascular late sequelae in long-term survivors of childhood cancer”) Reaching these milestones as well as further publications in high ranking scientific journals show the importance of the GHS and foster the CTVB strategy to enhance research in the field of cardiovascular biology at the UCMC.

It is of special importance to the CTVB to support a successful development of the DZHK and its structures/projects at the UCMC to ensure a long-term membership in this consortium. The funding body (BMBF) intends to establish a platform for outstanding collaborative research in the field of cardiovascular biology and clinical practice in the next years. The support strengthens the integration of the UCMC into this important national network. The funding for DZHK structures is long-term enterprise (starting in 2015; after re-evaluation in 2014). Within the research program at the UCMC, a large prospective cohort study on patients with heart failure was initiated in January 2013 to investigate the interaction between myocardial and vascular function; by end of 2013 approx. 750 subjects have been included in the trial. Furthermore, a prospective study on patients with suspect of acute coronary syndrome was prepared (for further information see the part DZHK on page [3]).

The CTH was structurally fully established in 2012 and the CTVB supported the fast build-up of an excellent infrastructure (method platforms) to enhance research in the field of thrombosis, hemostasis and cardiovascular biology. The CTH was able to not only further establish excellent new groups (the four newly established CTH professorships attracted further high profile PIs), joint projects between researchers from the CTH and other institutions of the CTVB demonstrate the strong potential of this strategy. The CTH was able to acquire a large-amount of additional third party projects, including a Humboldt-professorship (granted in 2013), large industry-funded clinical studies (HoSP, granted 2013), but also patient-oriented research projects (e.g. Bridging therapy in oral anticoagulation).

Within the CTVB, an awareness campaign was initiated promoting the prevention of cardiovascular disease: The Dept. of Medicine 2, the CTH and the Stiftung Mainzer Herz established the “Kinderakademie”, a school program for children and adolescents with a special emphasis on cardiovascular risk factors. The presentation and offer of the “Herz-Kreislauf-Spiel”, a game to playfully study the function of the cardiovascular system, was continued. A new research focus on the effects of noise (especially aircraft noise) on cardiovascular health was added to the portfolio of the CTVB. This topic is of great regional relevance and allows the CTVB to further contribute to important information on public health.

SPOKESPERSON: Professor Thomas Münzel

Spokesperson: Professor Thomas Münzel
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DESCRIPTION OF RESEARCH CENTER
FOR TRANSLATIONAL VASCULAR BIOLOGY (CTVB)

The CTVB demonstrates the strong potential of this strategy. The CTVB was able to acquire a large-amount of additional third party projects, including a Humboldt-professorship (granted in 2013), large industry-funded clinical studies (HoSP, granted 2013), but also patient-oriented research projects (e.g. Bridging therapy in oral anticoagulation).

Within the CTVB, an awareness campaign was initiated promoting the prevention of cardiovascular disease: The Dept. of Medicine 2, the CTH and the Stiftung Mainzer Herz established the “Kinderakademie", a school program for children and adolescents with a special emphasis on cardiovascular risk factors. The presentation and offer of the “Herz-Kreislauf-Spiel", a game to playfully study the function of the cardiovascular system, was continued. A new research focus on the effects of noise (especially aircraft noise) on cardiovascular health was added to the portfolio of the CTVB. This topic is of great regional relevance and allows the CTVB to further contribute to important information on public health.

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Biomaterials, Tissue and Cells in Science (BioMatics)

Artificial implants are now used in almost every surgical discipline. Examples include pacemakers, joint prostheses and implants serving as artificial tooth roots. Fundamental problems still consist in the interaction with the human body: Both a too weak adhesion of the implants as well as defense reactions of the body can affect the success of treatment. The same aspects apply to implants which do not replace bone but soft tissue, such as mucosa or blood vessels.

A number of working groups clinically and scientifically active surgeons at the University Medical Center Mainz in recent years established, dealing in interdisciplinary projects with the interaction of tissue and cells with exogenous materials. They work closely with the material scientists at Mainz University and the Max-Planck-Institute for Polymer Research. They also cooperate with other national and international partners from industry. Because it can be assumed that implants and associated problems at a steadily aging population are becoming more and more important, encourages the state of Rhineland-Palatinate these initiatives and cooperation since this year as a research priority “BIMatics - Biomaterials, Tissues and Cells in Science”. In the long term BIMatics be developed into a firmly anchored in the Mainz University internationally recognized center of gravity with its own young talent.

The integration in TransMed with a series of lectures, which can be seen in the internal portal ILKUM, represents a first step towards strengthening the linkage with the material sciences of the University and the Max-Planck-Institute for Polymer Research. It is clear that, so far mostly in materials science developments are triggered from the basic science viewpoint and in future a clinical viewpoint additionally required. The “surgeon scientist”, can help to provide effective development of smart and individual materials and lead to a synergy with a focus on “materials” of the University.

A milestone is the request of a graduate college of the German Research Foundation (DFG). Scientists from BIMatics are involved in a collaborative research center in cooperation of chemistry and medicine, University of Mainz University.

Spokesperson:
Professor Bilal Al-Nawas

Selected Publications | Max. 5

CRC 1080 Molecular and Cellular Mechanisms of Neural Homeostasis

Spokesperson: Professor Robert Nitsch

In recent years, research into homeostasis in the nervous system has gathered significant momentum. What is more, with its move to the centre stage of scientific research, it is now considered by many to be a “hot topic”. With this in mind our initiative has tasked itself with gaining a new understanding of the molecular and cellular mechanisms underlying the ability of the nervous system to maintain a balanced and stable internal state (homeostasis) when faced with constant input from an ever-changing environment. This ability is undoubtedly the most remarkable feature of the nervous system and by unravelling the mechanisms involved, we will provide a new basis for research into regeneration that will factor in both the attempt of neural tissue to regain its equilibrium in reaction to an insult, as well as the failure of these stabilizing mechanisms in progressive disorders. Our initiative is confident in its research and scientific discussions making a significant contribution to a clearer understanding of the concept of neural homeostasis. Moreover, this new understanding of the impact of homeostatic mechanisms and their potential pharmacological regulation will provide a new solid basis for novel therapeutic strategies.

Steering committee:

Robert Nitsch (spokesperson): Johannes Gutenberg University Mainz

Amparo Acker-Palmer (deputy spokes-

person): Goethe University Frankfurt

Heiko Luhmann: Johannes Gutenberg

University Mainz

Jochen Roepel: Goethe University Frankfurt

Miro HH Schmidt: Johannes Gutenberg

University Mainz

Erm Schuman: Max Planck-Institute for Brain Research

Participating Institutes:

Johannes Gutenberg University Mainz

Goethe University Frankfurt

Max Planck-Institute for Biophysics

Max Planck-Institute for Brain Research

Institute of Molecular Biology Mainz

IMB Project

Activity-Dependent Regulation of Apo-

tosis in Developing Rodent: Heiko Luhmann

Bioactive Phospholipid Signalling in

Homeostatic Regulation of Neuron Numbers

and Connections: Johannes Vogt / Robert Nitsch

A3 EGFL7: A Novel Modulator of Neural Homeostasis in the Hippocampus: Miro HH Schmidt/Stephan Schwarzacher

A4 Homeostasis of the Main Offactory Epi-

theleum in Mouse: Peter Mombaerts

A5 Defining the impact of newborn neurons in mouse olfactory bulb on neural homeos-

stasis by combining optogenetics with in vivo imaging: Albrecht Stroh / Benedikt Berin-

nath

A6 Epigenetic DNA Demethylation in Adap-

tation and Stability Processes of the Neo-

ravous System: Christof Nielsen/Bezt Lutz

A7 Functional Role of the Proteasome and Autophagic Protein Degradation System in Neuronal Homeostasis Following Traumatic Brain Injury: Kristin Engelhardt/Thomas Mitt-

mann/Christian Behl

A8 Stabilisation of the Neuronal Homeosta-

sis by Adaptation of Chaperone Activity to Long Term Protagenic Stress in vivo: Alb-

recht Clement/Christian Behl

A9 Programmed in the Adaptive Response of the Nociceptive System to Damage: Irmgard Tegeder

A10 GDAP1 is a exo sensor that controls cellular redox homeostasis by altering mito-

chondrial shape and function: Axel Mezher

B1 Decoding Neural Activity by Sypnic Proteome Remodeling: Erich Schuman

B2 Optogenetic and Ultrastructural Analy-

sis of Synaptic Vesicle Homeostasis at Hyper-stimulated Synapses in Caenorhabdit-

ei: sains: Alexander Gotschalk

B3 Molecular Mechanisms of Synaptic Adaptation after Denervation: Andreas Vo-

cho/Thomas Deller

B4 Molecular Mechanisms of Dendritic Development and Maintenance: Amparo Acker-Palmer

B5 Plasticity Related Gene 1: Functiona Role in Homeostasis of Synapse Formation and Maintenance: Robert Nitsch/Jisen Huai

B6 Molecular mechanisms of neuronal homeostasis during inflammatory processes in the CNS: Michael Schaffer/Franke Zipp

B7 Mechanisms of Homeostatic and Allos-

tatic Electrophysiological States of Dopa-

mineergic Midbrain Neurons in Aging and Models of Parkinson’s Disease: Jochen Roepel

B8 Endocannabinoids in Negative Feed-

back Mechanisms: Implications of Epigenetic Mechanisms Underlying Homeostasis and the Shift to Allostasis: Beat Lutz

SELECTED PUBLICATIONS | MAX. 5

Crassel CM, Dielme C, de Grooth RE et al. RNA Helicase DDX3 Is a Regulatory Subunit of Cae
denaxis 1 in Wnt-β-catenin Signaling. SCIENCE. 2013 Mar 22;339(6126):1346-41.


Nikolic I, Stankovic ND, Bcker F et al. EGFL7 Tages a3B3 Integrin to Enhance Vessel Formation. BLOOD. 2013 Apr 11;121(15):3041-50.

CRC/TRR 52 Transcriptional Programming of Individual T-Cell Subsets

Spokesperson: Professor Edgar Schmitt

In this project, we aim to unravel the molecular mechanisms underlying the complex differentiation processes of the many different subtypes of T-cell subsets. Hereby, we will focus on regulatory T cells (Treg), which are defined by their expression of CD4 and FoxP3. Tregs are found in a number of different in vivo compartments and play important roles in the control of immune responses. We will use a combination of advanced genomic, proteomic and functional approaches to define the transcriptional, protein-protein interaction and signaling networks that mediate Treg development and function. This will provide new insights into the regulatory mechanisms controlling Treg development and function. We will also investigate the role of Tregs in inflammatory and autoimmune diseases, and will develop novel therapeutic approaches to target Treg activity in these diseases.

SELECTED PUBLICATIONS | MAX. 5


Bacher N, Raker V, Hofmann C et al. 2013. Interleu-50 suppresses CD5 to disas-

se human regulatory T cells. CANCER RES. 73(18):5647-56.

Fig. 12: Transcriptional Programming of Individual T-Cell Subsets: The expression of a gene is controlled at regulatory elements within a given DNA locus called promoters. Gene expression (transcription) starts upon formation of the initiation complex that consists of multiple general and specific transcription factors binding to these promoters. Concomitantly, regulatory sequences (enhancers, repressors) upstream or downstream of the transcription start site can further modulate gene expression (adapted from Molecular Biology of the Cell, 2008).

DESCRIPTION OF CRC/1080

DESCRIPTION OF CRC/TRR 52

Long term research aim and common scientific interest:

The long term research aim of the TRR 52 is to gain new scientific insights into the func-

tion of T-lymphocytes through the intensifi-

cation of scientific research on the transcriptional control of gene expression in this vital population of lymphoid cells. Therefore, it is the aim to merge the different fields of expertise and laboratories in Würzburg, Mainz and Berlin, each of whose work is devoted to different aspects of T-cell biology. The expected fin-

dings are intended to significantly broaden our insight into the regulation of Gene expression in lymphocytes, one of the funda-

mental steps in the control of the immune system and, thus, to contribute to rendering the development of causal therapeutic approaches to frequent diseases of the immune system, above all auto-immune disorders and allergies, in future.

Projects (Mainz):

A1: Transcription Factors of Murine Regula-

A2: A analysis of Differential Gene Expression and Signal Transduction in Human Regulatory T Cells. PD Dr. A. Tüttene-

berg & HD Dr. H. Jonuleit, Dermatology, Mainz & Prof. A. Sickmann, Rudolf Virchow Center, Würzburg.
CRC/TRR 128 Initiating/effector versus regulatory mechanisms in Multiple Sclerosis - progress towards unraveling and treating the disease

DESCRIPTION OF CRC/TRR 128

Multiple sclerosis (MS) is the most common chronic inflammatory disease of the central nervous system in the western world and it leads to devastating disability in young adults, with only limited treatment options currently available. The socioeconomic burden of this disease is tremendous, since healthcare costs are very high and it affects decisions young patients must make for the rest of their lives. Findings in patients are a complex composite of inflammation (with demyelination, remyelination, axonal/neuronal damage) typically in subcortical, but also cortical, disseminated lesions and neurodegeneration. Remissions of clinical relapses point to the repair capacity of the CNS, which exhibits strong interindividual and course-dependent differences.

The Transregional Collaborative Research Center (CRC/TRR 128) is a consortium of scientists from institutions in the Rhine-Main Neuroscience Network (rmn2), Münster, Bochum and Munich, who are sharing their complementary scientific expertise and research resources as well as their clinical experience to achieve the goal of gaining novel insights into the pathology of MS and ultimately translating this to therapeutic improvements for patients.

The University Medical Center plays a central role in the CRC/TRR 128 with Prof. Frauke Zipp (Department of Neurology) acting as its spokesperson, as well as the principal investigators Prof. Ari Waisman (Institute of Molecular Medicine), Prof. Tobias Bopp (Institute of Immunology), Prof. Helmut Jorineit (Dermatological Clinic), Dr. Volker Siffrin (Department of Neurology) and Dr. Florian Kurzec (Institute of Molecular Medicine) being based here.

SELECTED PUBLICATIONS | MAX. 5


RU 926 Physiology and Pathophysiology of the Endocannabinoid System

The Research Unit FOR 926 “Physiology and Pathophysiology of the Endocannabi- nod System” was established in 2008. The two joint spokespersons are Prof. Andreas Zim- mer (Bonn) and Prof. Beat Lutz (Mainz). FOR926 is made up of working groups from Mainz (Prof. Behl, Prof. Lutz), Mannheim (Prof. Treede) and Bonn (Prof. Zimmer, Prof. Todt, Prof. Fleischmann, Prof. Schlieder). One central project in Mainz (Prof. Lutz) involves the qualitative and quantitative measurement of endocannabinoids by means of mass spectroscopy (LC-MS/ MS). The device was purchased within the context of FOR926 and is intended to be used also for further collaboration agreements apart from FOR926.

Endocannabinoids are lipids (fat-like substances) fulfilling important signal functions in the body. As the name already leads one to suppose, there is a connection with canna- bioids, the psychoactive substances from the hemp plant Cannabis sativa. In 1964, Δ9-tetrahydocannabinol (Δ9-THC) was identified as the psychoactive substance in can- nabis. In the following years, researchers tried to clarify the mode of action of Δ9-THC which led to a scientific breakthrough in 1990 with the discovery of the cannabinoid receptors and the subsequent identification of endogenic cannabi- nodoids, the so-called endocannabinoids.

In the past 15 years, numerous physiological processes have been identified in the body which are regulated by endocannabi- nodoids and cannabinoid receptors, such as, for example, fear behaviour, coping with stress, eating behaviour, inflammatory processes, sensation of pain, energy balance, heart and lung functions, and much more. The endocannabinoid system has protec- tive functions in many physiological situations and is thus positive for the organism. However, under pathological circumstances, the activity of the endocannabinoid system can be changed permanently, thus, for example, after long-lasting stress or in the case of adiposity. This changed activity of the endocan- nabino-system may contrib- ute to pathological processes.

The Research Unit’s objective is to examine the principle of the functionality of the endocannabi- nod system in a multidisciplinary approach in various model systems (e.g. mouse, pig, sheep, inflammation, pain, Alzheimer’s disease, bone homeostasis, heart and lung functions).

In addition, the pharmacological modulation of the system offers new therapeutic possi- bilities of being able to treat a series of pathologies. This is also intended to be explored in this research group.

DESCRIPTION OF RU 926

Spokesperson: Professor Beat Lutz

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The research unit RU 1341 “Barrel Cortex Function” began in 2010. This project is supported by the German Research Foundation (DFG) and the Swiss National Science Foundation. The spokespersons are: Prof. Heiko Luhmann (Mainz) and Prof. Friség Helmhchen (Zürich).

- Prof. Dirk Feldmeyer (Jülch)
- Prof. Carl Petersen (Lausanne)
- Dr. Poulet / Prof. Brecht (Berlin)
- Prof. Schwarz (Tübingen)
- Prof. Luhmann (Mainz)
- Prof. Helmhchen (Zürich)

**Scientific background:**

The cerebral cortex is organised horizontally in layers and vertically in cortical columns. Although the structural and functional properties of a cortical column have been intensively studied in a variety of mammalian species, the “canonical circuit” of a cortical column and the interaction between different columns is still largely unknown. Over the past few years, it has become clear that understanding neocortical information processing does not only require a detailed knowledge of the synaptic circuitry at the single cell level, but also an in-depth analysis of the columnar network activity at the population level. The rodent barrel cortex offers unique opportunities for studying sensory processing in a cortical column and for correlating whisker-related behaviour with neuronal activity in a well-defined cortical map.

The overall aim of this Swiss-German Research Unit is: Understanding the function of a neocortical column by using the rodent barrel cortex as a model for neuronal information processing within a neocortical module. The specific objectives are:

- To describe the inhibitory and excitatory synaptic circuitry within a barrel-related cortical column and to understand the general principles of neuronal information processing, i.e. excitatory feedback circuits within a cortical column.
- To study large-scale network activity in order to reveal the role of intracolumnar and intercolumnar interactions in spontaneous and sensorily-driven activity patterns.
- To examine defined synaptic microcircuits and large-scale neocortical networks during UP and DOWN states in order to elucidate state-dependent modifications of neuronal information processing.
- To understand the neocortical network mechanism participating in or generating a distinct sensor-related behaviour. To understand the processing of task-specific neuronal signals.
- To understand the activity-dependent mechanisms that lead to the formation of a cortical column during the pre-critical period and its modification during subsequent developmental stages.
- To develop, test and install novel behavioural tasks which will allow detailed electrophysiological or population imaging analyses of behaviourally relevant neocortical circuits.
- To develop novel techniques to monitor single cell and neuronal network activity in freely moving animals in co-operation with our two industrial partners and our international partner in Taiwan.

**SELECTED PUBLICATIONS | MAX 5**


**RU 1341 Barrel Cortex Function**

**DESCRIPTION OF RU 1341**

**RTG 1043 Immunotherapy**

The GRK 1043 “Immunotherapy” was conducted by members of the University Medical Centre and of the Faculty of Biology. Its second and final funding period ended in June 2013. An extension for a 1-year period was granted by the German Research Council on a regular basis and started in July 2013. This allows fellowship holders to finish their thesis work. The graduates programme aimed at the development of innovative immunotherapeutic approaches for the treatment of chronic inflammatory diseases, e.g. autoimmune as well as allergic and infectious disorders, and cancer. The GRK promoted the education and training of biologists (MSc) and medical doctors (MD degree) in basic and clinical immunology within an interdisciplinary and interfaculty training programme given in English. In 2013, 18 fellowship holders, 8 associated PhD students and 6 medical students participated in the programme’s activities.

**These were**

- Three ongoing core programmes (METHCoRe, IMMCoRe, PROCoRe) with weekly literature and progress reports seminars and obligatory laboratory rotations, with all the participants undergoing a written examination within IMMCoRe in 2013;
- A 2-day workshop entitled “Selfpresentation and Karrierausrichtung”, held in June 2013 for male participants within the programme’s advancement-of-women activities;
- A 1-day training workshop to improve presentation skills, held in November 2013 by Dr. Herzer (Zentrum für Qualitätssicherung, Marz University);
- Within the 7th Summer University “Biology & Immunology” in August 2013 34 high school students, nominated by their science teachers, spent two weeks in the GRK-associated laboratories, carried out laboratory work in small groups under the supervision of programme fellows, attended lectures given by project leaders and fellows, and presented their results on posters.

Six PhD students left the programme in 2013. Four students defended their PhD thesis, three with “magna cum laude” and one with “summa cum laude”. Three students defended their medical thesis. No new students could be accepted by the programme due to the end of funding.

External seminar guests were Dr. Christina Zielinski (Charité, Berlin) as well as Prof. Burkhard Becker (Experimental Immunology, University of Zurich).

**SELECTED PUBLICATIONS | MAX 5**


**DESCRIPTION OF RTG 1044**

Neuropathological modifications reacti-
genate genetically determined programmes and activity-dependent (repair) processes similar to those occurring during normal early development. This central idea is di-
essed in our interdisciplinary graduate school embracing different model organ-
isms (C. elegans, Drosophila, mouse/rat, human), using modern molecular biologi-
cellular physiological and clinical methods, including imaging techniques. In section A „Ontogenesis of the Nervous System“ (6 projects), basic mechanisms of cell migra-
tion, apoptosis, axonal growth, axon-glia interactions and the role of endo- and e-
ronal processes will be analysed. In section B „Neu-
rodegeneration and regeneration“ (6 pro-
jects) the molecular mechanisms of pathophysiological mechanisms in neuro-
degenerative processes will be analysed including developmental processes.

The successful course programme, which was developed during the first funding period, will be continued and extended by the inclusion of collaborative projects. This course programme consists of the component „demand“ (early preparation of project outlines and progress reports, organisation of meetings of the graduate schools by the doctoral students, training in the preparation of grant applications etc.), as well as of the component „pro-
mote“ (early presentation of scientific results at international meetings, support of visits to foreign labs, training in commu-
nications skills, scientific writing etc.).

**SELECTED PUBLICATIONS | MAX 5**


genic columns in the newborn rat barrel cortex. CEREbral CORTEX 23: 1299-1316.

**DESCRIPTION OF “BIOSILICA” AND “SI-BONE-POC”**

A considerable progress was achieved by the result that biosilica is a material that is not only biocompatible, osteoinductive and showing self-repair properties but also sui-
table for 3D printing. Moreover, this material is incorporated into bioactive hydrogels, turned out to be suitable for 3D cell printing. Based on these results we succeeded to successfully apply, together with a consortium in China, for a joint Euro-
pean-Chinese EU FP7 project on „Biomate-
rals: Imaging and rapid precise prototyping technology for custom made scaffolds“ (acronym „BioScaffolds“, grant no. 604036, duration: 2013-2016) in the NMP-3-2013-EU-China Call on „Biomaterials: Ima-
ing and rapid precise prototyping technology for custom made scaffolds“. The PI’s team could demonstrate that sponges which have both a light generating system (luciferase) and a light perception system (cryptochrome) are able to flash “in vivo”, indicating the existence of a nerve-ke system in sponges that use the spicules as light transmitters. In addi-
tion, a system controlling the day-night rhythm in sponges (nocturnin) has been dis-
covered. The discovery of the processes of biosintering, precision biosilica molding, and biosilica ageing allowed the development of new applications in nanobiotechnology and biomechanics. The development of nano-
bio-mechanical approaches based on biosilica for the treatment of bone diseases was sup-
ported by an additional ERC Proof-Of-Concept grant “Si-Bone-Poc” awarded to the PI of this ERC project.

First animal experiments with a biosilica-
based material (biosilica/silicatein-contai-
ning microspheres) revealed a significant improvement of bone healing. Recently, we could demonstrate that not only bone formation but also biocalcification (forma-
tion of calcium carbonate) of the calcare-
sous sponges is an enzymatically driven pro-
cess, mediated by a carbonic anhydride. Further results revealed that enzymatic (carbonic anhydrase-mediated) biosilica formation also plays an important role in human bone formation.

ERCA 2013-eu-china call on “Biomaterials: imaging and rapid precise prototyping technology for custom made scaffolds”. An ERC Proof-Of-Concept grant “Si-Bone-Poc” is awarded to the PI of this ERC project.

This ERC Advanced Investigator Grant project started in 2011 and will run until 2016. The ERC Proof-Of-Concept grant has been granted in 2013.

Biomineralization has attracted increasing scientific attention, not only because this process touches the interface between the organic and the inorganic world but also because it offers fascinating bio-inspired solutions in the fields of biotechnology and biomechanics. The marine sponges, the oldest still extant Meta-zoa, have a skeleton made of biosilica, a unique material consisting of polymeric silicate that turned out to be of extraordinary interest not only in nanotechnology but also in bone tissue engineering. Biosilica is the main mineral component of the sponge skeletal elements, the spicules. The formation of the spicules involves a sequence gene expression and is the first biomineralization process that can be described from gene level to biomo-
ecular to hierarchically ordered structures of increasing complexity, as shown by the ERC Investigator group. The special feature of this biomorphic material is that it is synthe-
sized enzymatically, at low precursor concen-
trations and ambient conditions. The responsible enzymes, silicateins, are the first and still only known enzymes that are able to catalyze the formation of an inorga-
nic hard material, biosilica, with quartz glass-like purity, from monomeric precurs-
ors (silicic acid). In 2013, we succeeded to elucidate the function of further proteins involved in the biosilification process, and in the processing (hardening) of the initially formed soft biosilica material, as well as the molecular switch (self-cleavage of pro-sili-
cateins) that results in the formation of enzym-
atically active and assembly-competent mature silicatein (acquisition of structure-
guiding and structure-forming properties). Moreover, the PI’s team could demon-
strate that sponges which have both a light generating system (luciferase) and a light perception system (cryptochrome) are able to flash “in vivo”, indicating the existence of a nerve-ke system in sponges that use the spicules as light transmitters. In addi-
tion, a system controlling the day-night rhythm in sponges (nocturnin) has been dis-
covered. The discovery of the processes of biosintering, precision biosilica molding, and biosilica ageing allowed the development of new applications in nanobiotechnology and biomechanics. The development of nano-
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sous sponges is an enzymatically driven pro-
cess, mediated by a carbonic anhydride. Further results revealed that enzymatic (carbonic anhydrase-mediated) biosilica formation also plays an important role in human bone formation.

**SELECTED PUBLICATIONS | MAX 5**

Müller WE, Schröder HC, Schöttmacher U, et al. Induction of carbonic anhydrase in 3D cell cultures of smad-2 cells, exposed to bicarbonate and consequences for calcium phospho-
ate crystal formation. BIOMATERIALS 2013; 34 (34) 8671-8680.


Wang KH, Schröder HC, Fang GQ, et al. The deep-sea natural products, biogenic polyphenols (bio-phenyl) and biogenic silica (bio-silica) as biomimetic scaffolds for bone tissue engineering: Fabrication of a morphogenetically-active polymer. MARINE DRUGS 2013; 11: 718-746.
The European Research Council (ERC) has earmarked about €2.5 million to fund the research being conducted by gastroenterologist and biochemist Professor Dr. Detlef Schuppan at Mainz University Medical Center. Professor Schuppan is a specialist in intestinal and liver diseases ranging from inflammation to fibrosis and organ failure and cancer. Among others, his aim is to develop therapeutic strategies that will slow or even reverse the pathological deposition of fibrous connective tissue (scarring) in various organs. Many patients could benefit from this development, because the advanced stages of fibrosis can currently not be treated and represent the main cause of death in those suffering from chronic inflammatory diseases of the liver and other organs. Ongoing inflammation usually leads to replacement of functional tissue by excess connective tissue (scarring) and the failure of organs like liver, lungs, kidneys or skin. Antifibrotic therapies to treat progressive fibrosis are lacking. While several antifibrotic drug candidates have been found in cell and animal studies, none has entered an advanced clinical phase. A major reason is the usually slow progression of fibrosis and the unreliability of follow-up tissue biopsy for the assessment of fibrosis progression (fibrogenesis). With current efficacy measures, “proof of concept” antifibrotic drug trials will have to include several hundred patients and to last at least 2 years, which incurs a high risk for patients and unacceptable costs for drug developers. Therefore, sensitive and specific non-invasive biomarkers are urgently needed. The project aims at the development of a quantitative imaging technology that permits the quantification of fibrous tissue deposition over the whole liver. The feasibility of this approach has been shown by research conducted by Professor Schuppan in collaboration with Prof. John Frangioni at Harvard Medical School, Boston (Prof. Schuppan was appointed at Mainz University Medicine still holds a professorship at Harvard). They developed an imaging agent (radiotracer) that binds to the fibrogenic cells in the liver. Injection of this radiotracer could visualize the activity of fibrosis progression in this organ. In collaboration with Prof. Frank Rösch and Junior Prof. Tobias Ross of the Institute of Nuclear Chemistry at Mainz University these and several other fibrosis imaging agents will be further developed and optimized, with the final aim of application in patients in 3-5 years from now. Notably, this method will allow 1) clinical efficacy testing of antifibrotic therapies in only a few patients within a few days to weeks, 2) an individualized dose adjustment of such therapies according to the therapy response.
German Cancer Consortium (DKTK)

DESCRIPTION OF GERMAN CANCER CONSORTIUM (DKTK)

The University Cancer Center (UCT, Mainz), along with its partner site in Frankfurt (UCT Frankfurt), is one of eight partners nationwide within the German Cancer Consortium (DKTK) “Deutsches Konsortium für Translatorsche Krebsforserung”). By its Institute of Medical Biostatistics, Epidemiology and Informatics (IMBE), the UCT Mainz is a key provider within both, the DKTK subcommittees on Cancer Prevention, Detection and Outcomes as well as the Clinical Communication Platform (CCP-IT). The Department of Hematology, Oncology, and Immunology as well as the Departments of Dermatology and Neurology contribute strongly to the immunotherapy program of the DKTK.

Immunotherapy

Adaptive cell therapy (ACT) with T cells retinoic acid transduced with tumor-associated antigen (TAA)-specific T cell antigen receptors (TCR) is a promising approach for immunotherapy in cancer patients. However, a safety concern of TCR gene transfer is the risk of pairing between introduced and the naturally expressed endogenous TCR chains that could result in the formation of new TCR heterodimers that can potentially be self-reactive (off-target autoimmunity). Along off-target reactivity, high-affinity, self-reactive TCR may also cause on-target toxicity for normal cells expressing low level of antigens.

The overall aim is to develop an effective, TCR-deficient tumor immunotherapy for wide-spread use in cancer patients by generating novel optimized specific T cell antigen receptors (TCR) by utilizing autologous, patient-specific TCRs. This approach is based on the use of autologous TCRs that are specific for tumor antigens and can be used to eliminate tumor cells without adverse effects. The main focus of this research is to develop an effective, TCR-deficient tumor immunotherapy for wide-spread use in cancer patients by generating novel optimized specific TCRs by utilizing autologous, patient-specific TCRs. This approach is based on the use of autologous TCRs that are specific for tumor antigens and can be used to eliminate tumor cells without adverse effects.

German Center for Cardiovascular Research (DZHK)

DESCRIPTION OF DZHK

The "German Center for Cardiovascular Research (DZHK)" is one of the six German centers of health research (Deutsche Zentren der Gesundheitsforschung (DZG)) established by the German Federal Ministry of Education and Research in order to explore and prevent widespread cardiovascular disease. The University Medical Center of the Johannes Gutenberg-University Mainz (UMMC) with its focus on epidemiology of cardiovascular disease is part of the DZHK in the location Rhein-Main.

Study procedure

Baseline Examination: Every eligible participant is invited to a comprehensive baseline examination with an echocardiographic examination in 2D and 3D, Cardiob Ultrasound Imaging, measurement of the endothelial function, body plethysmography, spiro-ergometry, standardized measures of blood pressure, 12-channel-ECG, anthropometric data, ABI, augmentation index, blood withdrawal, 24-hour ECG, 24-hour blood pressure and a computer-assisted personal interview (CAPI). The baseline examination takes place.

Follow-up 1: One year after enrollment into the study every participant is interviewed by means of a computer-assisted telephone interview (CAI).

Follow-up 2: Examination in the MyoVasc- Study Centre similar to the baseline examination after two years.

Follow-up 3: Computer-assisted telephone interview (CAI) in the third year.

Follow-up 4: Examination in the MyoVasc- Study Centre similar to the baseline examination in the fourth year.

Sample size

About 4.000 study participants from January 2013 to January 2017.

Data analysis

Cross sectional and longitudinal data analysis, case-control-studies.

Funding

The study is conducted as investigator-initiated trial and funded by the German Ministry of Research and Education within the DZHK-Zentrum Rhein Main in Mainz and by the Centre for Translational Vascular Biology.

Fig. 25: MyoVasc Study

Fig. 26: Department of Medicine II
Integrated Research and Treatment Center: Center for Thrombosis and Hemostasis (IBF CTH)

DESCRIPTION OF IBF CTH

A central goal of the BMBF-supported CTH is to develop a nationally and internationally visible center in thrombosis and hemostasis research. The center focuses on experimental, prevention and clinical studies in Mainz with Prof. Ulrich Walter as Scientific Director from 01/2012 - 09/2014.

Professorship for Translational Research in Thrombosis & Hemostasis (TR) Prof. Ulrich Walter, MD.

The major scientific goal of this professorship is the fundamental characterization of human platelets and their interaction with other human cells. Here, functional, biochemical, novel proteomic/phosphoproteomic and systems biology approaches are used. With the working hypothesis that platelets and the hemostasis system are circulating sentinels of vascular integrity it is aimed to improve the diagnostics and therapeutics of many still poorly-understood diseases in thrombosis and hemostasis.

Humboldt-Professorship/Translational Research (TR) Prof. Wolfram Ruf, MD, FAHA, Scientific Director

The Humboldt Professorship was created in 2013 and has expanded the scope of basic and translational coagulation research at the CTH. The basic science research program of the Professorship is focused on the signaling functions of the extrinsic tissue factor (TF) coagulation pathway in immunity, inflammation, metabolic disorders, and angiogenesis. The program addresses broadly disease processes dependent on the coagulation cascade, employing a repertoire of genetic model organisms in proof of principle mechanistic and preclinical studies. The expanding translational research program is built on deciphering the cell biology of the signaling and prothrombotic networks controlled by TF and the development of novel diagnostic and interventional strategies for assessing disorders of coagulation. These approaches aiming to validate pathogenic mechanisms in the clinics are expected to provide guidance and optimized interventional strategies for modulation of coagulation pathways in thrombosis, obesity, cancer progression, and immunological disorders.

Professorship for Experimental Hemostasis and Laboratory Medicine (ER) Prof. Sven Danckwardt, MD

The Module Experimental Hemostasis and Laboratory Medicine is mainly concerned with underlying molecular principles of (de) regulated blood coagulation and the resulting implication for diagnostics and therapy. In this context the module is interested in processes of posttranscriptional gene expression control and their role in the regulated (patho)physiology of blood coagulation, the connection to tumor biology and immunity. Applying an integrative approach, all scientific topics include elements of basic research (biochemistry, molecular and cellular biology), modeling of diseases in animals and finally understanding the translational implications in patients. Complemented by the successful implementation of preclinical optical imaging, we will illuminate such processes on a systems level non-invasively in living subjects.

Professorship for Clinical Trials (CT) Prof. Stavros V. Konstantinides, MD, PhD, FESC, Medical Director

The Professorship and Module Clinical Trials supports the leading role of the CTH in (inter)national scientific collaboration and networking with a focus on venous thromboembolism. The Module's research projects and multicenter trials are integrated into the overarching translational research focus of the CTH on the transition from acute to chronic thrombosis. The Module helps to shape leading-edge patient care in thrombosis and hemostasis, both locally, within the Health Care Center of the CTH and internationally, by coordinating the task forces of national and European guidelines on the management of pulmonary embolism.

In 2014/2015 four Junior Groups within the CTH program are successfully established:

- Junior Group „Translational Research“ (Christoph Reinhardt, MD)
  - Junior Group „Vascular Biology“ (Phil Wenzel, MD)
  - Junior Group „Clinical Trials“ (Maneke Lankeit, MD)
  - Junior Group „Experimental Research“ (Markus Bomsann, MD)

The University Cancer Center (UCT Mainz) provides the framework for education, prevention, diagnosis, treatment, and psycho-social care of cancer patients with in the University Medical Center. The UCT also oversees clinical, translational, and basic cancer research as well as local, national, and international cancer research programs on oncology. Founded in 2011, the UCT is responsible for designing the interfaces between the entire medical disciplines involved in the care of cancer patients at the University Medical Center. Interdisciplinary tumor boards for the variety of cancer entities lay the basis for rational diagnostic and therapeutic decision making for almost every individual cancer patient. A clinical cancer registry is part of the UCT Mainz and responsible for diagnostic, therapeutic, and outcome data collection and evaluation.

In 2013, the structural requirements and resources for comprehensive cancer tissue and liquid biobanking have been set up. The sampling of cancer patient biomaterials will be operative in late 2014 and thus provide another step forward to high quality cancer research at the University Medical Center Mainz. Also in 2014, outpatient medical service to cancer patients will be performed within a dedicated, central UCT facility. Along with the UCT Frankfurt, the UCT Mainz is a partner within the German Cancer Consortium (DKTK).

SELECTED PUBLICATIONS | MAX 5

Mayer G, Vrucut E, Lankel M, Konstan

Dellas C, Tscheppe M, Seeber V, Zwen
ner I, Meyer G, Vicaut E, Lankeit M, Kon

Bock F, Geiger J, Walter U, Zahedi RP. Time-resolved characterization of cAMP/PLA2-dependent signaling reveals that platelet inhibition is a concerted process elevated pka-dependent signaling reveals that platelet inhibition is a concerted process elevated pka-dependent signaling reveals that platelet inhibition is a concerted process elevated pka-dependent signaling reveals that platelet inhibition is a concerted process elevated pka-dependent signaling reveals that platelet inhibition is a concerted process.

Yokota N, Zarpellon A, Ruggeri ZM, Ruf W. Contributions of thrombin targets to tissue factor-dependent metastasis in hyper-

Interdisciplinary Center for Clinical Trials (IZKS)

IZKS is a professional university-based clinical trial institution of the University Medical Center Mainz (UMC) which contributes to quality and efficiency of clinical trials by competence and appropriate infrastructure. IZKS integrates clinical trial management and methodological trial competence in an interdisciplinary structure generating synergies for strengthening clinical research of the UMC.

IZKS is one out of only five centres at German universities whose implementation and development is funded by the Federal Ministry of Education and Research (BMBF) for continuous optimization of multicentre clinical trials, for building regional trial networks and for improving qualification of staff personnel and thereby contributing to the progress of clinical research in Germany.

To adhere to international scientific and ethical clinical trial standards and to comply with the respective legal requirements, thorough knowledge, skills and tools for clinical trials have been established. Compliance with quality standards and Good Clinical Practice (GCP) has been confirmed in several audits and in a GCP-inspection by the local authority. In addition, success and achievements have been assessed repetitively resulting in excellent appraisals ("very good, excellent") and subsequently in further extension and many new grants for research projects.

Strength and portfolio of IZKS:
- Comprehensive trial expertise for drug- and medical device studies as well as for other trial interventions, such as surgical and psychotherapeutic procedures
- Successful grant applications in cooperation with clinical scientists to BMBF, DFG, EU, DAI and pharmaceutical and medical device industry
- Full scope of clinical trials operating functions according to ICH-GCP, e. g. study coordination, regulatory affairs, clinical monitoring, quality management, data- and safety management, biostatistics, electronic trial systems & processes
- Complete fulfillment of all sponsor liabilities in Investigator Initiated Trials (IITs)
- Professional Clinical Trial Units
- Qualified study staff
- Quality management according to GCP
- Education and training for investigators, scientists, study nurses, monitors and medical students
- Authorization to train, educate and examine Medical Doctors to acquire board certification in clinical pharmacology
- IZKS is a member of the German KKS network (www.kks-netzwerk.de), surgical network (www.chir-net.de) and the TMF („Telematik Plattform für Medizinische Forschungsnetze“, TMF: www.tmf-ev.eu).
- Furthermore, IZKS established cooperation with 16 academic and several non-academic hospitals, private physicians, study groups, competence networks in medicine, European Clinical Research Infrastructures Network (ECRIN) and with pharmaceutical and medical device industry which demonstrates acceptance and recognition of IZKS.

KEY RESEARCH AREAS

Focus of IZKS is planning, preparation, management, evaluation and publication of prospective, randomized, controlled clinical trials (RCTs) investigating the following interventions:
- Drugs
- Medical devices
- Surgical procedures
- Psychotherapeutic procedures

Special expertise is implemented for IITs and the respective sponsor duties according to GCP and in the performance of all specified sponsor tasks. In addition to RCTs, competence has been expanded to health care research, registries and EU research projects resulting in a collaboration of IZKS with four EU projects.

SELECTED PUBLICATIONS | MAX. 5


Head: Professor Monika Seibert-Grafe
University Medical Center Mainz Langenbeckstr. 2 D-55131 Mainz phone: + 49 6131 17-9913 seibert-grafe@izks-mainz.de
www.izks-mainz.de

Fig. 30: IZKS staff

Fig. 31: Strength & Success through Partnership

IZKS Services comprise:
- Consulting, planning and coordination of clinical trials
- Development of study protocols and other Essential Trial Documents according to ICH-GCP
- Project management according to GCP
- Conduct of trials with qualified and experienced investigators and study nurses
- Clinical monitoring in Germany as well as in other neighbouring European countries
- Regulatory & quality management
- Fulfilment of Sponsor obligations on behalf of the University Medical Center
- Audits and reviews of trial documents
- Safety management and pharmacovigilance including accredited electronic reporting to EUDRAVIGILANCE
- Biostatistics
- Data management
- Data validation and query management
- Internet-based 24-hours randomization
- Reports and publications
- Certified trainings for clinical trial staff

IMPORTANT PROJECTS | MAX. 5

CE RTI Fly - Ceramic Treatment of Fracture Defects: A prospective, multicenter, randomized study investigating the use of CE RAMENT™ (Bone Void Filler R) as bone graft substitute in Tibia Plateau Fractures
Project Manager: Prof. PM Rommens, Dr. S. Gorbulke
Cooperation: Opher Nomhoff (BONE SUPPORT GmbH)
Funding: BONESUPPO RT GmbH
Project Duration: 2012 - 2014

child-EU (HC O / EAA )
Project Manager: Prof. M. Gross, Dr. K. Kronfeld
Cooperation: Ludwig-Maximilians-University Munich (Pediatric Pneumology)
Funding: EU € 3.000.000
Project Duration: 2012 - 2016

Home Treatment of Patients with Low Risk Pulmonary Embolism With the Oral Factor Xa-Inhibitor Rivaroxaban (Hot-PE)
Project Manager: Prof. S. Konstantinidis
Cooperation: Prof. M. Möckel University Medical Center Charité Berlin, CC 13; Internal Medicine with Gastroenterology and Nephrology, Emergency/Rescue Stations, Dr. F. Klein-Waigl Chest Pain Units, HELIOS Klinikum Berlin-Buch, Angiology, Prof. U. Rauch-Kröhnert, University Medical Center Charité Berlin, Campus Benjamin Franklin, CC 11: Cardiovascular Medicine, Department of Medicine II – Cardiology and Pneumology et al.
Funding: Federal Ministry of Education and Research
Project Duration: 2013 - 2018

Funding: Bayer AG
Sum: € 1.850,000
Project Duration: 2013 - 2016

Interstitial Center for Clinical Trials (IZKS) (Federal Ministry of Education and Research)
Project Manager: Prof. M. Seibert-Grafe
Cooperation: Other Universities, national (Charité Berlin, Universities Bochum, Essen, Frankfurt, Leipzig, Tübingen and Ulm) and international (Belgien, Nederland, Osterreich, Schweiz, USA), Educational Hospitals and non-academic institutions, national (Hospital Bad Kreuznach, Catholic Hospital Mainz), Hospital Ludwigshafen, Dr.-Horsl Schmidt-Hospital Wiesbaden (Industry, international, Study-Group and Network, national (Working-Group Interna Ophthalmology (AOO), German Foundation of Organ Transplantation (DSO), Research Association Musculoskeletal Diseases, Competence Network COPPS/Asthma, Competence Network Diabetes mellitus, Makroevoludics Institute) and Central European Society for Anticancer Drug Research (CESAR)
Funding: Federal Ministry of Education and Research
Project Sum: € 8.787,281
Project Duration: 2007 - 2015

Resolution of Left Atrial-Appenage thrombus - Effects of Dabigatran in patients with AF (RE-LATED AF)
Project Manager: Prof. T. Münzel, Prof. T. Rostock, Dr. M. Fehrer et al.
Cooperation: University Medical Center Mainz (Department of Medicine II), APNET (Competenznetzwerk Arrhythmia)
Funding: Boehringer Ingelheim GmbH & Co. KG
Sum: € 650,000
Project Duration: 2013 - 2018
SELECTED PUBLICATIONS | MAX 5


The NIC is a core research platform of the Medical Faculty. The NIC provides assistance with neuroimaging in humans to all interested parties at the University Medical Center as well as to cooperation partners within the Focus Program Translational Neuroscience (FTN) in Mainz. Regular users include the departments of Neurology, Psychiatry and Psychotherapy, Nuclear Medicine, Physiological Chemistry, Psychomotor Medicine and Psychotherapy, Microscopic Anatomy and Neurobiology (all University Medical Center) and Clinical Psychology and Neuropsychology (Institute of Psychology).

The NIC has at its disposition research-only scanning time on a 3 Tesla Siemens Tim TRIO magnetic resonance (MR) scanner (located in building 605 on medical campus), equipment for peripheral stimulation, psychophysiological recordings, eye-tracking, transcranial direct current stimulation (DCS), combined MRI-EEG, two fully equipped psychophysiological laboratories for behavioral studies (in building 503), dedicated Unix and Windows servers, analysis software, and an office suite with terminals for data analysis in building 701. Services include regular methods teaching activities, advice with study design, ethics applications, stimulus presentation, sequence selection, data analysis, and bi-weekly discussion meetings. From 2017, the NIC will be housed in a new dedicated neuroimaging building that will harbor a new 3 Tesla MR scanner, an EEG suite, other laboratories and office space for imaging groups from the faculty and FTN.

Imaging the human brain is a way to study the neural basis of human cognition and behavior, to unravel mechanisms of neurological or psychiatric disorders, and to develop methods for the prevention and treatment of those conditions. We mainly use magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS), noninvasive, safe and comparatively inexpensive techniques that exploit the natural presence in the body of protons and other nuclei with a “spin”, that is, which we can see by applying phasic radiofrequency pulses while the body is in a strong static magnetic field (e.g., 3 Tesla). We thus generate images of brain structure (grey and white matter, cerebrospinal fluid, fiber tracts), brain chemistry (concentrations of certain brain metabolites), and brain function (changes in perfusion when brain areas are active during certain experimental conditions). Especially functional imaging allows us to observe the living human brain “in action” and relate those measures to behavior, learning and memory, subjective experience such as perception, thoughts or feelings, to personality, genotype, or pathology. We can also assess changes in brain structure, chemistry or function as a result of pharmacological, psychological/behavioral, neurotechnological or therapeutic interventions.

NIC users investigate questions like multiple sclerosis, aging and dementia, addiction, impulse control, emotion regulation, executive function, fear and anxiety, and aesthetics. The NIC professorship (Raffael Kalisch), together with its collaborators, has a particular interest in the topic of resilience. Resilience describes the process of maintaining or regaining one’s mental health during or after severely stressful life situations. Traditionally, psychiatric research has focused on mechanisms that make people vulnerable and lead to disease and on ways of treating mental illness. Interestingly, however, many people do not or only temporarily become mentally ill despite significant burden from psychological or physical adversity. This suggests the existence of protective mechanisms that can prevent the development of stress-related conditions like anxiety, post-traumatic stress, depression or addiction. Our approach is to understand these resilience mechanisms and to harness them in the service of better disease prevention. This strategy can potentially much reduce individual suffering, dysfunction and economic and social costs. Here, neuroimaging is a key tool to gain insight into the brain mechanisms underlying and promoting resilience.
Translational Animal Research Center (TARC)

DESCRIPTION OF TARC

The Translational Animal Research Center is responsible for all aspects of housing and breeding of laboratory animals at the University Medical Center Mainz. Thereby the major tasks lay in the breeding of genetically modified mouse strains and the housing of experimental animals, as well as health and genetic monitoring of the animal units.

In addition, the TARC operates a biotechnical laboratory in which embryo rederivation for health restoration of mouse strains, genetic “back up” of mouse strains by cryopreservation of embryos or sperm and also DNA microinjection to generate transgenic animal strains, plus stem cell injections to produce homologous recombined mouse variants are performed.

KEY RESEARCH AREAS

A current research project is the TARC telemetry project entitled „Acquisition of the severity of distress and pain of laboratory animals by telemetric determination of physiological reactions“, promoted by the Stifting Rheinland-Pfalz since 2011. The foundation runs until 2014. As part of the project standard experimental procedures, e.g. administration of tetracycline in the drinking water, will be investigated by the impact of distress and pain of laboratory mice. The severities of distress, pain and suffer are measured by the telemetric detection of the body temperature, heart rate and motility.

The main purpose of the autonomous training platform for general medicine (Teaching Department for General Medicine) under its director Prof. Michael Jansky, is, as the name suggests, to provide teaching. The training platform concentrates on the main activities of a general practitioner providing care to a non-specialized group of patients. The areas covered and forms of training provided are: Career exploration, an introduction to clinical medicine, interdisciplinary subject Q12 (rehabilitation, manual therapy and complementary medicine), a course in general medicine, a block internship as well as a year’s practice in general medicine.

The research projects undertaken by the training platform correspondingly focus on these tasks. The primary research focus of the general medicine training platform is in the fields of practice-oriented health care research, postgraduate training programs and educational research with particular reference to general medicine.

The main research projects of the Teaching Department: General Medicine include a practice-oriented health care research program (in cooperation with the Institute of Medical Psychology and Medical Sociology and the Rhineland-Palatinate Association of Statutory Health Insurance Physicians), post-graduate training programs and educational research (concentrating on the assimilation of clinical and preclinical training and interactive teaching).

Practice-oriented Health Care Research
A project on the subject of "Emergency care provided by on-call general practitioners from the point of view of the participants" is currently in progress and should be completed by the end of 2013. Among the themes of this project are the expectations that patients have when they visit a medical emergency service center at the weekend or at inopportune times. This project is also looking at why patients take advantage of this service. As part of this project, on-call physicians are also being asked for their views of the emergency which resulted in the use of their services. A new project in the field of health services research is concerned with the relevance of 24-hour blood pressure monitoring in practice. It is planned to conduct a study in cooperation with the Rhineland-Palatinate Association of Statutory Health Insurance Physicians focusing on the initial diagnoses, the frequency of use, the relevance of 24-hour blood pressure monitoring in practice and the associated therapeutic strategies. Following discussions with the Association of Statutory Health Insurance Physicians, the benefits of collaboration for both partners were identified and long-term cooperation in this field was proposed. We hope to be able to initiate more joint projects with the Association of Statutory Health Insurance Physicians in the near future.

The other projects are mainly in the field of health care research with a view to improving teaching practices related to the block internship and practical year. This involves close cooperation with the Institute of Medical Psychology and Medical Sociology.

Further joint projects in this area are planned for the future. Following initial contact and initiation of projects (still at the planning stage) with the Association of Statutory Health Insurance Physicians, the members of the training platform have decided to continue to conduct research in the field of health care.

As announced in last year’s research report, a postgraduate training program project has been designed that includes a multi-media, interactive training DVD, which is now shortly before publication.

Postgraduate Training
A postgraduate training project that is currently in its final stages is the follow up to last year’s training DVD on "Identification of HIV infection by GPs". The aim of the current study is to determine the training needs of general practitioners or internists in the area of post-exposure prophylaxis after needle-stick injury or unsafe sex. As in the case of the precursor project, an interactive DVD has been produced that enables these to test their own knowledge in the field and also provides corresponding training material on the subject. The purpose of the project is thus not merely to identify the needs but also to simultaneously cover those needs and to fill existing gaps in knowledge. Additional copies of the training DVD created as part of the prior project had to be produced this year to meet the considerable demand. We hope that the follow-up project will be similarly successful.

Educational Research
Last year's project on the subject of "Use of a voting system in seminars on general medicine" has been finalized. Another educational research project currently at the planning stage concerns the integration of preclinical and clinical training. One of the most important tasks of general practitioners is to explain, in simple terms, the often complex situations that arise in medicine. This very often requires basic knowledge in the fields of physiology, anatomy and physiological chemistry. In collaboration with the Institute of Physiology and the Rudolf Frey Learning Clinic, a corresponding learning/teaching concept for the new preclinical course is currently in the progress of being prepared.

SELECTED PUBLICATIONS | MAX 5
Kau U. Why aren’t more General Practitioners happy about their work? MMW. 2013, 2: 25

Fig. 35: 24h blood pressure monitoring in practice
Fig. 36: DVD „Carenlos - now what?“ Research into patient care combined with training
Fig. 37: Introduction to clinical medicine. Assimilation of clinical and preclinical training

IMPORTANT PROJECTS | MAX 5
HIV in general practice
Project Manager: Prof. B Schappert, Prof. M Jansky
Project Duration: 2010 - 2015

Improve teaching in general medicine
Project Manager: Prof. M Jansky, Prof. B Schappert
Project Duration: 2010 - 2014

Integration of preclinical and clinical teaching
Project Manager: Prof. M Jansky, Prof. R Haidmayer
Project Duration: 2011 - 2014

Postgraduate training
Project Manager: Prof. M Jansky, Prof. B Schappert
Project Duration: 2011 - 2015
Mainz Research School of Translational Biomedicine
(TRANSMED)

Program Director:
Professor Esther von Stebut-Borschitz

The Mainz Research School of Translational Biomedicine (TRANSMED) and its doctoral degree regulation PhD-MD/PhD in Translational Biomedicine were jointly established in 2012 by four faculties of the Johannes Gutenberg University (JGU) Mainz, the University Medical Center, Biology, Chemistry/Pharmaceutical Sciences/Geosciences and Social Sciences/Media/Sports.

TRANSMED plays a multifaceted role for the promotion of young scientists in life sciences at JGU Mainz and at cooperating institutions in the Rhine-Main area. TRANSMED serves as the graduate school for the Research Center “Translational Medicine” with its three research areas “Immunotherapy (F3)”, “Translational Neurosciences (FT1)” and “Translational Vascular Biology (CTV)”. In the end of 2013, the translational training program of JGU’s Research Unit “Bio-materials, Tissues and cells in Science (BiomasTICS)” was integrated under the roof of TRANSMED.

Beyond this, TRANSMED is the umbrella organization for all training groups within the area of biomedicine at JGU and offers an attractive curriculum with maximum flexibility in translational research for both physician scientists and natural scientists.

This curriculum comprises a qualification concept that enables MD/PhD, PhD and Dr. rer. nat. students to complete their degree within 36 months. The students are required to obtain 180 credit points in total. The work on the research project corresponds to about 85% of the time invested in the doctoral studies (150 credit points). Further 20 credit points are offered for technical training and interdisciplinary education and 10 credit points for multidisciplinary skills.

In 2013, the first five TRANSMED Fellows have been selected through a competitive application procedure. The fellows are co-supervised by a clinician and a basic research scientist.

Two of the TRANSMED Fellows are physician scientists who perform a MD/PhD thesis in parallel to their specialist training. The support by TRANSMED allows them to perform their research project for half of the duration of the fellowship. The other three TRANSMED Fellows are natural scientists performing a PhD or Dr. rer. nat. thesis. They will be familiarized with the workflow at a clinical institution and introduced to the regulatory issues of patient-oriented research.

The Postdoc Community

The University Medical Center’s Postdoc Community is an informal association of postdoctoral fellows. Since 2010, the members specifically aim to create a network among all postdocs and provide information on funding and career development. In this context the Postdoc Community organizes events and provides the chance to exchange views on career opportunities.

In 2013, various Postdoc Community events took place. Prof. Ignaz Wessler from the Ethics Committee Rhine-Land-Palatinate, introduced research ethics guidelines that need to be followed when planning research involving human participants. As project management is a basic requirement for successful research projects, the Postdoc Community organized a certified multi-day training on this topic. Moreover Sandra Helinski gave a lecture in May, which provided hands-on experience on project management. Another lecture held by Dr. Johanna Mazur and Aslihan Gerhold-Ay, gave insight into statistical methods that help to organize and analyze large sets of data. In November, Dr. Andreas Strecker tried to answer the question how to obtain extramural funding by the German Research Foundation (DFG).

All events organized by the Postdoc Community have in common that they address the whole group of young scientists, no matter what specific discipline they belong to.

All postdocs at the University Medical Center Mainz are welcome to participate and can contact Dr. Angela Clement for further questions on the Postdoc Community.
Pre-clinical Institutes

- Institute of Functional and Clinical Anatomy
- Institute of Microscopic Anatomy und Neurobiology
- Institute of Physiology
- Institute of Pathophysiology
- Institute of Physiological Chemistry
- Institute of Pathobiochemistry
I. Teaching
The Institute offers a number of events for students of medicine and dentistry, such as a macroscopic anatomy course (dissection), a course on microscopic anatomy (histology course), and lectures and seminars. The teaching accomplishments of the institute have been recognized through the award of the Teaching Prize of the State of Rheinland-Palatinate (R. Spessert, 2008) and the Johannes Gutenberg-University Mainz (R. Spessert, 2013). The head of the department is one of the three authors of the “Prometheus LernAtlas Anatomie”, “Lernkarten Anatomie”, “Lemnaket Schädel” and co-author of the textbook “Duale Reihe Anatomie”.

II. Research
The research carried out focussed on the subjects angiogenesis, wound healing and tumour growth, as well as circadian systems, the retina, gene expression and the daily dynamics of the photoreceptor cells. The methodological repertoire of the research groups includes a wide spectrum of microscopic techniques (e.g., scanning electron microscopy, transmission electron microscopy, laser scanning microscopy, in addition to biochemical (e.g., Western blot, Southern blot) and molecular-biological techniques (e.g., Real-time PCR, gene-deficient mice models).

Research Group Konerding:
The reparative and regenerative wound healing depends, among other things, on the induction of blood vessels. New vessels are formed either through the sprouting of pre-existing vessels or through intussusceptive angiogenesis (IA). Within the framework of a NIH-R01 cooperative project, our group investigated to what extent the IA is involved in the new formation of murine lung tissue after pneumonectomy and whether it can be influenced. The mechanisms of lung growth, and in particular the participation of endothelial progenitor cells are being investigated together with our cooperation partners at the Brigham and Women’s Hospital of the Harvard Medical School and the Harvard School of Public Health. In addition, the influence of micromechanical forces during regeneration was investigated using a unilateral phrenic exeresis. Working in close cooperation with the Fraunhofer Institute for Industrial Mathematics (ITWM), 3D quantification methods using MAVI-software were used in order to collect information on vessel volume density, vessel surface, diameter, and the Euler number.

Within the framework of this project, this platform should be optimised and further developed in order to investigate the influence of physical factors (mechanical stress) and endothelial progenitor cells on the post-pneumonectomy lung growth. This project developed as a result of our investigations on chronic inflammations, in which we were able to show that microangioclastia with drastic reductions of the shear forces are a structural prerequisite for the migration of leukocytes. In two different colon inflammation models it was possible to prove that after measurement of the diameter of the capillaries in the submucosal plexus, duplication of the vessel distance occurred, preferably through intussusceptive growth. In addition, the Konerding research group also further investigated the effects of proangiogenic growth factors such as VEGF (vascular endothelial growth factor), PDGF (platelet-derived growth factor and FGF-β (basic fibroblast growth factor), as well as endothelial precursor cells on wound healing with the aim of an optimized wound healing. In addition, in cooperation with the University of Ulster the effects of angiogenesis in Alzheimer’s disease and its therapeutic influence.

Clinical questions concerning the biomechanics of the ventral body wall, the integration of hernia meshes or jarring injuries are being worked on in various clinical cooperations.

Research Group Spessert:
The retina is subject to a daily rhythm with regard to numerous parameters. This diurnal regulation is - in the case of the vertebrae - highly conserved and functional and can be used as an adaptation to the changing light intensity which occurs more than 100 times over the 24-hour daily cycle. The daily adaptation of the retina also applies to the photoreceptors (rods and cones). In this way they show a 24-hour rhythm with regard to their morphology (e.g., renewal and phagocytosis of the membrane discs in the outer segment, ultrastructure of the ribbon synapse) and physiology (e.g., synthesis of melatonin, visual signal processing). The daily changes in the photoreceptors are partly directly regulated through the outer light conditions and partly through the retina’s own molecular clocks (oscillators), which on their part are influenced by the outer light conditions. In the research group, the daily adaptation of the photoreceptors is being investigated at the gene level. Here, the working hypothesis is tested that the survival of photoreceptors under changing light intensities is promoted by the daily regulation of genes protecting possessive power.
The Institute for Microscopic Anatomy and Neurobiology was established in Dec. 2009 and is located on the second floor of building 708 at the University Medical Center along with the research unit of the Department of Neurology and the Central Laboratory Animal Facility (CLAF). Following its successful setup period, it is now home to the research groups of Prof. Robert Nitsch (WD), Prof. Mirko H. Schmidt (W2) and Prof. Albrecht Stroh (W1). The Institute houses facilities for biochemistry, molecular biology, histology, state-of-the-art imaging (confocal microscopy, two-photon microscopy in vitro and in vivo), electron microscopy and experimental animal models (e.g., brain tumor models, electroporation in utero). The institute is part of a tight international research network and cooperates with the Focus Program Translational Neurosciences (FTN), the Research Center for Immunotherapy (FZI) and the Center for Thorbmosis and Hemostasis (CTH). Together with the groups of the neuroscience communities in Mainz and Frankfurt it forms the rhine-main-neuroscience network (rnn2). Members of IMAN also participate in the CRC1080 "Molecular and Cellular Mechanisms of Neural Homeostasis" and the initiative CRC1146 "Targeting inefficient immunity in malignant and chronic infectious diseases". From January 2018 the institute will move to the Biomedical Research Centre located on the Johannes Gutenberg University Campus, where it will be in direct proximity to the Institutes of Physiological Chemistry, Physiology & Pathophysiology and Pathobiology as well as the research facilities of the FTN. The Institute of Molecular Biology (IMB) will also be located in the vicinity.

Prof. Robert Nitsch research focus:

1. The role of bioactive phospholipid signaling in the nervous system: A precise understanding of the molecular mechanisms of layer formation and connectivity in the developing brain as well as the homeostatic control of signaling in the adult brain can provide a basis for possible therapeutic interventions in brain disorders. The significance of bioactive phospholipid signaling by LPA and LPA-receptors for cortical layer formation, connectivity and synaptic homeostasis has only recently been recognized. This signaling pathway involves the LPA-synthesizing enzymes autotaxin and the post synaptic regulators PRG-1/2. In order to explore the members of the LPP-superfamily various transgenic mouse lines have been generated, which show distinct phenotypes including overexacitation at the glutamatergic synapse. Cell-based assays, molecular structure analysis, morphological techniques including high-resolution microscopy and electron microscopy as well as in utero electroporation and various mouse models are applied to understand the function of this signaling pathway.

2. Axonal outgrowth, axonal reorganization and neuroimmune interaction: The second focus addresses the question of the involvement of non-neuronal cells in the process of CNS reorganization. The brain as an immune-privileged organ has long been thought to broadly ignore self-response in the CNS is not only associated with axonal damage but also with remission in the course of multiple sclerosis. Understanding mechanisms of axonal transport and signaling is thus a main focus of our research.

3. Neuroaesthetics: This new field of research addresses cognitive processes underlying adaptation in the arts. A combined view from humanities and neuroscience on recognition and perception of adaptations is pursued. Neuroaesthetic correlates are studies using functional imaging using various perception paradigms.

Prof. Nitsch has also secured from the European Research Council (ERC) some EUR 2.5 million to fund his research. Liquid Signaling at the Glutamatergic Synapse: Involvement in Brain Network Function and Psychiatric Disorders "LipsyD". The "Molecular Signal Transduction" labs focus on the analysis and cure of CNS diseases. Questions of life sciences and translational research approaches are applied to contribute to the cure of patients. Particularly:

1. How malignant brain tumors, e.g., glioma are formed and how they can be treated beyond conservative medicine is studied in the framework of the German Consortium for Translational Cancer Research (DKTK). The Research Group “Molecular Imaging and Optogenetics” focuses on combining state-of-the-art optogenetic techniques with optical neuroimaging. Advancement of our understanding of neuronal network dynamics in health and disease requires the investigation of defined populations of neurons and their interactions in the intact CNS. Probing the specific contribution of genetically defined neuronal populations to network function is pivotal for furthering our knowledge of impairment of network dynamics and for the development of effective therapy strategies.

By applying approaches of systems biology, the MS labs study molecular signal transduction processes that are mediated by proteins, which are secreted or localized in the plasma membrane of cells. These molecular targets offer the advantage of being druggable from the cellular exterior. Examples of signaling modules analyzed are EGF/Lotch-, EGF/EGFR- or integrin-mediated signaling pathways. The MS labs cover a broad range of life science techniques ranging from biochemical analyses via advanced imaging and lab animal models to the analysis of human specimens.

Juniorprof. Albrecht Stroh research focus:

1. How malignant brain tumors, e.g., glioma are formed and how they can be treated beyond conservative medicine is studied in the framework of the German Consortium for Translational Cancer Research (DKTK).

2. How neural stem cells are regulated in the adult brain, whether these cells can be exploited for the cure of neurodegenerative diseases, e.g., Alzheimer’s disease and which influence newborn neurons have for the homeostasis and allostasis of the adult brain. The latter is of particular interest for resilience disorders.

3. The molecular causes of neurovascular diseases, such as stroke, are explored and it is studied how these diseases can be prevented, cured or at least, how their detrimental effects can be attenuated.

By applying approaches of systems biology, the MS labs study molecular signal transduction processes that are mediated by proteins, which are secreted or localized in the plasma membrane of cells. These molecular targets offer the advantage of being druggable from the cellular exterior. Examples of signaling modules analyzed are EGF/Lotch-, EGF/EGFR- or integrin-mediated signaling pathways. The MS labs cover a broad range of life science techniques ranging from biochemical analyses via advanced imaging and lab animal models to the analysis of human specimens.
The Institute of Physiology was formed recently by separation from the former Institute of Physiology and Pathophysiology. The Institute of Physiology consists of the groups of Prof. Luhmann (development and physiology of cortical structures), Prof. Mittmann (plasticity and pathophysiology of cortical structures) and the subgroups PD Dr. Kilb (cortical development and network interactions), PD Dr. Kirischuk (physiology of glial cell), Dr. White (molecular-biology and pathophysiology of glial cells) and Dr. Hedrich (blood-brain-barrier).

**Main Focus of Research**

The group of Prof. Mittmann studies the question how does activity from intracellular proteasome and autophagy signal cascades mediate adaptation and homeostasis in the somatosensory cortex following traumatic brain injury in mice. Another project addresses the function of GABAergic synaptic inhibition in the vicinity of focal lesions in the visual cortex. In a third project the role of the proteoglycan NG2 for neocortical brain function is investigated to better understand the role of oligodendrocyte precursors (OPCs), specifically the role of the proteoglycan NG2, for synaptic neurotransmission and cellular processes of learning an memory in mice.

The group of PD Dr. Kilb investigates the cellular physiology of the immature cerebral cortex and the role of developmental disorders in the generation of neuronal pathologies. Another project is focussed on the role of early network activity in the development and refinement of cortical structures and connections.

The group of PD Dr. Kirischuk investigates the information flow in the brain as a combination of “digital” (synaptic) and “analogue” (volume) transmissions by the use of electrophysiological, but also microfluorimetric, immunohistochemical and molecular methods.

The group of Dr. White studies with molecular biological methods myelination and remyelination processes. The goal is a better understanding of the molecular mechanisms governing myelogenesis, which may become instrumental in developing therapeutic approaches promoting remyelination processes in demyelinating diseases.

The group of Dr. Hedrich investigates the physiology and pathophysiology of the blood-brain-barrier in different in vitro models. Another goal is to develop novel nanoparticles, which may overcome this barrier to influence pathological processes in the brain.

**Important Publications**


**Important Projects**

- **Activity-Dependent Regulation of Apoptosis in Developing Rodent**
  - Project Manager: Prof. H. Luhmann
  - Funding: German Research Foundation
  - Sum: € 377,500
  - Project Duration: 2013 - 2016

- **Barrel Cortex Function / Development of a barrel-related cortical column in the newborn rat**
  - Project Manager: Prof. H. Luhmann
  - Cooperation: Prof. C. Petersen, Brain Mind Institute Ecole Polytechnique Federale de Lausanne Lausanne, Prof. D. Feldmeyer, Dept. of Psychiatry and Psychotraumatology RWTH Aachen University, Prof. E. Halmacher Dept. of Neurophysiology Brain Research Institute University of Zürich et al.
  - Funding: German Research Foundation
  - Sum: € 1,477,827
  - Project Duration: 2010 - 2015

- **Functional Role of the Proteasome and Autophagic Protein Degradation System in Neuronal Homeostasis Following Traumatic Brain Injury (BP A07) - SFB 1040)**
  - “Molecular and Cellular Mechanisms of Neural Homeostasis”
  - Project Manager: Prof. C. Bahl, Prof. K. Engelhardt, Prof. T. Mittmann
  - Cooperation: Prof. K. Engelhardt, Department of Anesthesiology, Prof. T. Mittmann, Institute of Physiology and Pathophysiology
  - Funding: German Research Foundation
  - Sum: € 442,400
  - Project Duration: 2013 - 2016

- **Molecular mechanisms of localised Myelin Basic Protein synthesis in oligodendrocytes (German Research Foundation)**
  - Project Manager: Dr. R. White
  - Cooperation: Dr. Stefan Tenzer, Institute of Immunology
  - Funding: German Research Foundation
  - Sum: € 226,432
  - Project Duration: 2013 - 2016

- **Propagation of neuronal assemblies in central networks (PAK 520) / Transfer of thalamocortical information and its control by GABAergic mechanisms in the adolescent mouse cerebral cortex in vitro (Partial project Luhmann / Kilb)**
  - Project Manager: Prof. H. Luhmann, PD Dr. W. Kilb
  - Cooperation: Prof. José Bargas, Instituto de Fisiologia, National University of Mexico, Prof. A. Dragoon Institute of Physiology and Pathophysiology, University of Heidelberg, Dr. M. Both, Institute of Physiology and Pathophysiology, University of Heidelberg et al.
  - Funding: German Research Society
  - Sum: € 276,500
  - Project Duration: 2011 - 2013
The Institute of Pathophysiology was formed recently by separation from the former Institute of Physiology and Pathophysiology. The structure of the new institute is currently in the process of reconstruction and renewal. In 2013, one research group in the new institute was continuously active in the field of basic and translational cancer research. This team has issued pioneering work on tumor metabolism and its interactions with the aggressiveness and therapeutic resistance of the disease. The scientific success was made possible by the development of unique technology for in situ quantification of metabolites. This method, termed "induced metabolic Bioluminescence Imaging: imBi", allows for the quantitative measurement of the tissue concentration of disease-relevant metabolites in relation to the histological tissue structure with a spatial resolution on a microscopic level. The use of substrate-specific enzymes as "biochemical sensors" for the metabolites warrants high sensitivity and specificity of the technique as well as the acquisition of biologically and clinically relevant data.

For several years and up to now, basic and clinical research on tumor metabolism has been permanently expanding which includes numerous clinical studies worldwide to exploit metabolic reprogramming within malignant tumors for therapy. Unlike molecular approaches, such a metabolic targeting is not directed toward a specific receptor or signaling molecule, but rather attacks the particular metabolic status of a cancer cell. There is an increasing number of recent reports on promising results of such strategies in the clinic.

Due to the successful application of their imBi-technique in experimental studies and in tumor patients, the tumor group in the Institute of Pathophysiology has received numerous requests for collaboration on a national and international level. One of such a collaborative study has been published in Nature in 2013. During that year, the group leader was an invited speaker at 2 national and 4 international congresses, among others, at the 25th European Congress of Pathology in Lisbon, Portugal.

In collaboration with the OncRay National Research Center at Dresden glycolysis-associated metabolites and mRNA levels were characterized in tumor xenografts from 4 human head and neck squamous cell carcinoma lines with various intrinsic radioresistencies during a fractionated radiation treatment. Significant changes in ATP and mRNA levels of glycolytic enzymes occurred already after 3 to 5 dose fractions in radioresistant but not in radioresistant tumors. These changes represent confounding parameters for pre-therapeutically induced lactate levels being a prognostic but not predictive marker of radioresistancy. On the other hand, the findings obtained suggest that personalization of radiotherapy may be improved by monitoring the ATP and transcriptional radiation response of tumors in an early treatment phase.

A second collaborative project with the OncRay Center and the Gesellschaft für Schwerionenforschung (GSI) Darmstadt was focused on differential cell biological effects of heavy ions compared to conventional x-rays. Using human glioma cells, one core result was that conventional, but not particle irradiation may induce an increase in cell motility in radiosensitive glioma cells. Such an effect may reduce the efficiency of a conventional radiotherapy, since irradiated cancer cells may become mobile and leave the irradiated target volume during fractionated treatment. As a consequence these cells may not receive the appropriate radiation dose and may lead to a recurrence of the disease. Thorensen seems to be absent with heavy ion irradiation.

In a collaboration with the Molecular Cancer Research Center of the Charité University Medical Center at Berlin we were able to make a significant contribution to the research on metabolism during therapy-induced tumor cell senescence. Using the imBi-technology an unexpected hypermetabolism with increased glycolytic activity was demonstrated to occur following induction of senescence. This phenomenon could be exploited specifically for therapy by certain inhibitors of the glycolytic pathway.

In the year of this report, the tumor group has initiated a collaboration with the Clinic for Neurosurgery of the University Medical Center of Mainz (Director: Prof. A. Giese). A program was set up for imBi-measurements in patients with gliomas. Preliminary results in primary glioblastomas indicate that these malignancies are characterized by a very high glycolytic activity and intensive lactate accumulation which has been shown in other tumor entities to be linked to aggressiveness and radioresistance. Unlike in other tumor types, such as cervix carcinoma, head and neck cancer or colon adenocarcinomas, tumors with a relatively low glycolytic rate has not been detected in glioma patients so far.

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The Institute of Physiological Chemistry consists of three research groups: “Molecular Mechanisms of Behavior” (Prof. Lutz), “Adult Neurogenesis and Cellular Reprogramming” (Prof. Beningo), “Applied Molecular Biology” (Prof. Müller/Schroeder/Wanger).

Together with the Institute of Pathobiology, we teach the subject “Biochemistry/Molecular Biology” for medical and dental students. In preparation for the first period of the medical exams (“Physikum”), a broad knowledge in biochemistry and molecular biology is conveyed by lectures, practical courses and seminars.

We also educate young academics (doctoral, master and bachelor students) from the Faculties of Biology, Chemistry and Medicine. We offer state-of-the-art laboratories, young and international teams, and innovative projects.

The close proximity to the Institute of Physiology and Pathophysiology, to the Institute of Molecular Biology (IMB), to the Institutes of the Faculty of Chemistry and Biology, and to the Max Planck Institutes of Polymere Research and of Chemistry opens numerous synergies between the various research interests directly on site.

The dynamic of membrane lipids and bioactive lipids in neurological processes using mass spectrometry techniques. The discovery of lipid signatures of various physiological and/or pathophysiological states, as well as the translation of neurobiological knowledge into quantitative assays for monitoring of changes in the endogenous levels of lipids and bioactive lipids in various tissues and bodily fluids associated with different neurophysiologic diseases, represent the main research activities of the unit.

Group “Adult Neurogenesis and Cellular Reprogramming”

This group led by Prof. Benedict Beningo investigates the mechanisms underlying how we learn and forget, how we are able to cope with stress (“stress resilience”) and why chronic stress can strongly affect our behavior (e.g. memory, social behavior, pain perception, eating behavior, energy metabolism). This behaviors are mostly controlled by the brain, but also by neuronal and hormonal interactions between the brain and peripheral organs. Behavioral patterns can also get engraved during development of the nervous system or by metabolic processes. Changes in behavior and in cellular processes can be observed under pathophysiological conditions. Under certain circumstances, these changes can lead to psychiatric or neurological diseases. We use a multidisciplinary approach to get new insights in these complex behavioral processes in the mouse animal model. This includes genetic, pharmacological, biochemical methods as well as methods of cellular and molecular biology, histology and electrophysiology.

In understanding these processes mentioned above, a major focus is put on the role of the endocannabinoid system, a local signaling system of the organism, on neurotransphins, and on epigenetic processes.

Our lipodynamics facility aims to investigate the olfactory dendroglial lineage by enhancing the proliferation of oligodendrocyte precursor cells, also referred to as NO2 glia. This suggests that distinct stem cell populations in the adult brain are amenable to selective expansion which may become relevant when aiming at recruiting stem cells for brain repair.

In another study, we were able to identify the temporal sequence of how neurons generated in the other main neurogenic region of the adult brain, the dentate gyrus of the hippocampus, become incorporated into the pre-existing neural circuitry (Deshpande et al., 2013). We could show that young neurons first become innervated by local inhibitory and excitatory interneurons and only later receive synaptic input from long-range presynaptic partners, such as the entorhinal cortex. On basis of these data, we propose a model according to which incorporation into the informatic processing stream is preceded by integration into a local circuit.

Group “Applied Molecular Biology”

This research group is led by Prof. Werner Müller, Prof. Heinz C. Schroeder and Prof. Xiaohong Wang, and investigates three topics.

Molecular Evolution: The focus is on the molecular biology of aquatic invertebrates, in particular sponges, to elucidate the origin of Metazoa about 700 million years ago. Functional studies on molecules of innate immunity, apoptosis, cell communication and morphogenesis shall contribute to the understanding of pathobiochemical mechanisms in humans.

Biomaterialization – Nanobiotechnology / Nanomedicine – Bioprinting: Biomaterialization processes, such as the formation of the sponge biosilica skeleton and human bone formation are investigated. Biosilica, a material of exceptional optical and mechanical properties, is formed by a unique enzyme-catalyzed mechanism. The aim of the ERC Advanced Investigator project "BIO multifunctional (Biol). Müller) is the development of novel applications of biosilica in nanobiotechnology (e.g. micro-optics and biomedicine (e.g. bone repair). Advanced 3D cell printing ("bioprinting") methods for the development of customized implants are used in the EU FP7 project "Bio-Scaffolds". Biomedical inorganic polymers like biosilica are also a topic of the Chinese-German Centre for "Bio-inspired Materials", coordinated by Prof. Müller and Wang (also coordinator of EU FP7 project "CoreShell").

Bioactive Substances: Marine sponges are a rich source of new bioactive substances. As part of the EU FP7 large-scale integrating project "BlueGenics", methods for the sustainable production of these compounds are developed, in particular for therapy of bone diseases (osteoporosis).

Fig. 44: Transsynaptic labeling of newly generated neurons in the adult dentate gyrus and their local presynaptic partners. Red fluorescence indicates newly generated neurons; green fluorescence reveals presynaptic partners of newly generated neurons; yellow labeling indicates cells onto which green presynaptic partner cells form synapses. The tracing technique is based on rabies virus transfer from post-to presynaptic partners (Deshpande et al., 2013).

Fig. 45: Bioprinting of bone-forming SAOS-2 cells in an alginate/gelatin hydrogel matrix (A) The bioprinted staks were overlaid with (B) agarose. The individual cells were visualized by staining of their nuclei with DRAQ5. (C) Printed layers, SEM.

**IMPORTANT PROJECTS | MAX. 5**

- Defining the impact of newborn neurons in mouse olfactory bulb on neural homeostasis by combining optogenetics with in vivo imaging
  - Project Manager: Prof. B Berringer, Junior Prof. A Stotz
  - Funding: German Research Foundation
  - Sum: € 414,400
  - Project Duration: 2013 - 2016

- Detection and quantification of endocannabinoids by LC-MS/MS FOR 926 CP1 LU 779/4-2
  - Project Manager: Prof. B Lutz
  - Cooperation: Prof. A Zimmer, University Bonn, Dr. J Allertke, University Bonn, Dr. K Morony, University Medical Center Mainz et al.
  - Funding: German Research Foundation
  - Sum: € 312,350
  - Project Duration: 2011 - 2014

- EU ERC Advanced Grant BIOBILICA (Individual grant; European Research Council; Grant agreement no.: 264676); From gene to biomineral: Biosynthesis and application of sponge biosilica
  - Project Manager: Prof. W Göller
  - Funding: EU FP7
  - Sum: € 2,183,600
  - Project Duration: 2011 - 2016

- EU FP7 – BlueGenics (Grant Agreement Number 311848) Large-scale integrating project: BlueGenics – From gene to bioactive product: Exploiting marine genomics for an innovative and sustainable European blue biotechnological industry (coordinator: W.E.G. Müller)
  - Project Manager: Prof. WE Müller, Prof X Wang
  - Funding: Cooperation: Prof. Dr. Christian Sauer, Münster, Prof. J Alferink, University Bonn, Dr. K Morony, University Medical Center Mainz et al.
  - Funding: EU FP7
  - Sum: € 1,370,920
  - Project Duration: 2012 - 2016

- SFB/TR 58: Fear, anxiety and anxiety disorders
  - Project Manager: Prof. B Lutz
  - Cooperation: Prof. HC Pape, Westfälisches Wilhelms-Universität Münster
  - Funding: German Research Foundation
  - Sum: € 279,400
  - Project Duration: 2013 - 2016
Institute of Pathobiochemistry

As one of the Basic Science Institutes of the University Medical Center, we are entirely committed to two endeavors: generating new knowledge, and conveying established knowledge to the next generation of physicians and scientists. In teaching primarily second year MD students the basic principles of natural science and molecular medicine, we want to ensure them with a true understanding of the etiquette, diagnosis and therapy of human disease.

Our scientific interest is directed towards the molecular origins of neurodegenerative disorders. In three research groups (Behl Group, Piestrzik Group, Moosmann Group), we focus on aging, oxidative stress, and protein homeostasis, as well as on pathogenetic processes especially of Alzheimer’s disease. Employing various experimental systems – cell culture as well as animal models (i.e. the nematode C. elegans and mammalian models) – we investigate Alzheimer’s and Parkinson’s disease and Amyotrophic Lateral Sclerosis, but also stroke and chronic hypoperfusion, all aimed at the development of new approaches towards prevention and treatment.

The Institute for Pathobiochemistry is participating in several coordinated research programs, namely the CRC “Molecular and Cellular Mechanisms of Neural Homeostasis”, the German Research Foundation (DFG) Research Units “Physiology and Pathophysiology of the Endocannabinoid System” and “Physiological Functions of the APP Gene Family in the Central Nervous System”, the DFG Research Training Group “Developmental and Disease-Induced Modifications of the Nervous System”, the Competence Network “Degenerative Dementias” and the German Networks for Mitochondrial Disorders (mitoNET) and Motor Neuron Diseases (MND-NET), as well as in the Research Center for Translational Neurosciences (FTN) Mainz and the Frankfurt Autophagy Network (FAN).

Fig. 46: C. elegans, Luc: GFP expression in muscle; APP23 mouse model, hippocampus, congo red (amyloid plaque) and hematoxylin (nucleus) staining; rat midbrain neurons, NeuN (neuron) and DAPI (nucleus) staining; fibroblast cell line MRR0, X-Gal (beta-galactosidase) staining (clockwise)

The most frequent neurodegenerative disorders are strongly associated with age. Consequently, we investigate how neurons age, how cellular biochemistry changes during aging, and how age-associated alterations affect the onset and course of neurodegeneration. Oxidative stress and mitochondrial dysfunction are two very characteristic features of neurodegeneration. Hence, we pursue the development of novel antioxidants and modulators of mitochondrial metabolism as neuroprotective strategies. Since many neurodegenerative disorders are defined by a disturbed homeostasis of the cell, in particular, autophagy, we have recently shown that this system is substantially influenced by the aging process. Employing C. elegans reporter lines and RNAi libraries, we are currently working on the identification of novel modulators of macroautophagy and characterize their impact on cell survival and neuronal function (“Biochemistry of Neurodegeneration and Aging”, Behl Group).

The pathological appearance consistent with neurodegeneration especially in Alzheimer’s disease (AD) shows intracellular, neurofibrillar tangles and extracellular plaques in the brain of affected patients. The “Molecular Neurodegeneration” Group (Piestrzik Group) is interested in the initial cellular processes that may lead to the development of the disease. Therefore we concentrate on a novel enzyme meprin β which may play a crucial role in the development of sporadic forms of AD by generating truncated amyloid β peptides (Aβ). A second focus of our research team lies on the blood-brain barrier which plays an essential role in maintaining the brain homeostasis, preventing the brain from uncontrolled entrance or diffusion of potentially harmful molecules. Several recent studies have highlighted the importance of this barrier in neurodegenerative diseases for instance by regulating transport of Aβ via the low density lipoprotein receptor related protein 1 (LRP1) in AD. Therefore, we are interested in the role of LRP1 as key receptor in Aβ transport across the blood-brain barrier.

The “Evolutionary Biochemistry and Redox Medicine” Group (Moosmann Group) is interested in how evolutionary mechanisms have shaped today’s biochemistry in the animate nature and in humans. On a molecular level, evolution has sculptured all biochemical pathways to varying degrees, including redox biochemistry, which is deeply intertwined with human disease. The elucidation of the causal factors that have moulded modern redox biochemistry might be of unique value for the understanding and treating of these human disorders. In this respect, our focus is on neurodegenerative diseases such as Alzheimer’s disease, pathologies influenced by the mevalonate pathway (leading to cholesterol and selenoprotein synthesis), and the general biological aging process.
Institutes of Clinical and Theoretical Medicine

- Institute of Occupational, Social and Environmental Medicine
- Institute of the History, Philosophy and Ethics of Medicine
- Institute of Immunology
- Institute of Medical Microbiology and Hygiene
- Institute of Pharmacology
- Institute of Legal Medicine
- Institute of Toxicology
- Institute of Virology
- Institute of Translational Immunology (TIM)
The Institute of Occupational, Social and Environmental Medicine represents the corresponding disciplines in research as well as teaching and provides consultancy service in the health care sector. Since 2001, a specialized advisory Institute for Teachers’ Health (IfL) was integrated in the institute. The institute currently employs a staff of 40 scientific and non-scientific workers. The interdisciplinary team consists, among others, of physicians as well as natural and social scientists, who enable a broad scientific spectrum. The independent disciplines Occupational, Social, and Environmental Medicine are subdivided into the working groups “Occupational Medicine”, “Occupational Toxicology and Laboratory Diagnostics”, “Occupational Physiology”, “Public Health/ Social Medicine”, “Occupational and Social Psychology”, “Environmental Medicine”, and “Teachers’ Health”. The Institute is involved in the excellence cluster of the state Rhineland-Palatinate with the topic “social networks and overcoming poverty and debt”. Since 2004 a partnership has been maintained between our Institute and the Universidad del Norte in Barranquilla, Colombia. A number of scientific activities took place as part of this partnership, which includes the International and Caribbean Congress on Environmental and Occupational Health in 2011. Over the last few years, the area of teaching has seen several innovative educational projects. One of these projects includes the conceptualization and filming of the professional training and retraining films “The Practice”, “The Workshop”, “Mобbing” and “Under Pressure” with support from the electronic media center of the Johannes Gutenberg University. The redesigned teaching block (9 SWV) “Social Medicine, Public Health and O3”, which was taught for the first time in December 2011, saw a refinement of its content and its “game based learning” unit. Moreover, the IfL offers student teachers an educational program (lectures and seminars) on the topic “teachers’ health” since the winter term of 2011/2012.

The major aim of the toxicological laboratory is to develop and apply analytical methods to determine pollutants and associated metabolites in biological material (biological monitoring). A current research project compares different matrices (e.g. plasma, serum, whole blood, urine, saliva) regarding a potential pollution with organic solvents. The results will be used to develop new strategies for biological monitoring. Further scientific projects focus on the individual susceptibility to effects of harmful substances.

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The Institute for the History, Philosophy and Ethics of Medicine researches and teaches at the intersection of theoretical and clinical medicine on issues of theoretical principles, historical developments and ethical implications of medical practices. On the one hand, the research foci address socially relevant and currently debated topics of health care (such as questions regarding individual health care and prevention), aiming at the utilization of research results, for instance in the area of medical ethics, for solving of problems in the clinical daily routine. A high level of practical relevance is assured by Prof. Norbert Paul’s chairmanship of the ethical committee and by the active implementation of ethical advising in the hospital. On the other hand, the Institute conducts foundational research in the closely interconnected branches of history, theory and ethics of medicine because the analysis of current issues in medical ethics and their evaluation requires a historical contextuality and a theoretical foundation.

The research library of the Institute is equipped with a non-circulation collection of more than 70,000 volumes (including journals, microfilm and -fiches, CD-ROM, manuscripts and other sources). The library consists of works on the history of medicine and the history of science from different eras, subject areas and research foci, among others on the topics of medical ethics, gender and health/illness, biologism and public health.

Gender images and concepts of prevention of cardio-vascular diseases in Germany, 1949-2000 (funded by the German Research Foundation)

Based on the premise that prevention concepts are constituted in a dialog between medicine and the general public, the research project explores the influence and scope of the socio-cultural context of prevention campaigns in relation to gender images. The aim of the medical-historical comparative analysis of specific body and gender images in prevention campaigns for coronary heart diseases in a German-German comparison between 1949 and 2000 is a historical explanation of the current disproportion between, on the one hand, the information on the risks of the diseases circulated via prevention campaigns and, on the other hand, the knowledge about these risks that the addressees’ of the campaigns have at their disposal.

History, Theory and Ethics of Medicine in public perception

The aim of the project is the evaluation of the cross-section 2 “History, Theory and Ethics of Medicine” regarding the scientific definition of teaching and learning outcomes of this thematic group within the medical curriculum. To this end, the project will ascertain the thematic areas taught at different universities and provide a comprehensive analysis of the literature on the subject matter. Ultimately, the success of teaching and learning will be surveyed and evaluated through a longitudinal quantitative and qualitative survey of students and alumni.

Patients, the general public and medicine in West Germany from 1945 to 1970 (funded by the German Research Foundation)

The project examines the social anchoring of scientific medicine in West Germany between 1945 and 1970. In three sub-projects, the research will focus on (1) the re-presentation of medicine in the magazines “Der Spiegel” and “Stern,” (2) the physician-patient relationship regarding diabetes and its representation in “Diabetiker”/Diabetes-Journal and (3) the physician-patient relationship in the Federal Armed Forces (1955-1970) and the public debate on this issue.

Biological Economies. A history (archeology) of growth (ca. 1770-1970)

The project on the “history (archeology) of growth” focuses on the buried interconnections between the discourses on growth and the bilateral references of economy and biology between 1770 and 1970. In addition, the project will reveal the biological roots and premises of economical models. In the context of this project, a workshop on the “Economies of Reproduction” was co-organized in Berlin in October 2011.
Institute of Immunology

The Institute for Immunology is a one of the basic research institutes at the University Medical Center Mainz. Its assignments are to conduct immunological basic research, to transfer research results into the preclinical phase and the close interaction with clinical partners for translation of these findings into clinical application. Preclinical disease models play a central role for this type of applied immunology. With their help, the findings that have been gained from in vitro studies can be checked for their possible therapeutic potential. In this regard, several preclinical tumor and asthma models were established at the Institute of Immunology. Using these models, several tumor-specific vaccination strategies as well as the influence of factors, which are formed by mast cells and helper T cells (Th9), to the formation and development of experimental asthma are examined currently. The close integration of molecular and cell biology in vitro experiments with studies in preclinical models can thus lead to innovative immunotherapeutic treatment measures. To support this research orientation a highly modern flow cytometry unit for the isolation of different cell populations ex vivo is as well established as a state of the art mass spectrometry unit for the identification of proteins and small molecules, particularly specialized in the label-free quantification of proteins and peptides. A fundamental requirement for the successful conduct of such studies is young, well-trained and motivated scientists. Therefore, the Institute of Immunology is working hard in educating and training students. We are also coordinating the immunological teaching program within the study of biology, pharmacy and biomedical chemistry.

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IMPORTANT PUBLICATIONS | MAX. 5


MAIN FOCUS OF RESEARCH

The research activities realized at the Institute for Immunology concern various aspects of the induction of innate and adaptive immune responses. As part of our investigations of the innate immune system we analyze the function and regulation of mast cells and neutrophils, as well as their interaction within the framework of the induction of inflammatory reactions and in the development of airway hyper-sensitivity. Our work on the activation of cells of the innate immune system and their effect on the induction of adaptive immune responses addresses particularly the use of ligands for Toll-like receptors in the development and optimization of vaccination protocols. The focus lies particularly on the control of the activity of different populations of dendritic cells in the skin and in peripheral lymphoid organs while tolerance and induction of antigen-specific immunity is established.

The studies on the activation of adaptive immune responses are completed by projects that attend on one hand with the role of different cytokines in the differentiation of T-cells and on the other hand with the function of regulatory T cells. The T-cell differentiation analyzes is focused on studying the regulatory mechanisms, which modulate the expression but also the inhibition of individual genes, such as transcription factors. These genes control the influence on the development and function of different T helper cell populations, such as Th2, Th9, Th17 cells. With respect to the function of regulatory T cells, the influence of these T-cell sub-populations for the activity of both dendiric cells and CD4 and CD8 positive T-cells will be analyzed.

Regulatory T cells play an essential role in maintaining the immunological balance. A subpopulation of these T cells promotes the development of allergic and auto-aggressive diseases while hyperactivity promotes the tumor development. For this reason, studies in understanding the inhibitory mechanisms of regulatory T-cells play a central role.

Studies that lead to a better understanding of antigen processing and presentation of MHC Class I ligands in tumors and virus-infected cells complete projects for a better understanding of activation of the adaptive immune system. Through international cooperation, we are particularly interested in the specificity of the proteasome system and cytotoxic and ER-resident aminopeptidases in the generation of MHC class I ligands in the context of HIV infection.

Fig. 49: Enzyme-linked immunosorbent assay (ELISA)

Fig. 50: Auto Sampler of a state of the art Mass Spectrometer
The Institute of Medical Microbiology and Hygiene is a part of the Research Center of Immunology and Immunotherapy at the University of Mainz Medical Center. It focuses on better understanding how multicellular organisms protect themselves against infections and how the commensal microbiota has established a mutualistic relationship with its host at border surfaces. The Institute also teaches microbiology and infection medicine to students of the School of Medicine, the School of Dentistry and the School of Pharmacy. It provides diagnostic and clinical consultant services in virology, infection medicine and antimicrobial stewardship for the University Medical Center.

**Main Focus of Research**

We, the scientists at the Institute of Medical Microbiology and Hygiene, aim to perform groundbreaking research into how multicellular organisms protect themselves against infections and how the commensal microbiota has established a mutualistic relationship with its host at border surfaces. We are eager to open new areas for research and approach unresolved issues in biology. Such new insights should fundamentally change our scientific thinking and may substantially contribute to future medical practice through the development of more efficient treatment methods to find a cure for debilitating diseases such as infections, cancer and auto-immune-driven diseases. We aim to achieve our vision by maintaining a focus on excellent research and by recruiting only the brightest scientists.

**Important Publications | MAX. 5**

**Hoyler T, Connor CA, Kiss EA, et al. (2013).** T-bet and Gata3 in controlling type 1 and type 2 immunity mediated by innate lymphoid cells. CURR OPIN IMMUNOL 25, 139-147.

**Kiss EA, Scherzer V et al. (2013).** A T-bet gradient controls the fate (HPV16) L2 and repress the long control region of HPVs. J VIROL 87, 4461-4474.

**Klose CS, Kiss EA, Schwierzeck V et al. (2013).** Transcription factor Ebf1 is essential for the maintenance of B cell lymphoid cells. Nature 494, 261-265.

**Mechanitzky R, Akbas D, Scherer S et al. (2013).** The Institute of Medical Microbiology and Hygiene teaches microbiology and infection medicine to students of the School of Medicine, the School of Dentistry and the School of Pharmacy. It provides diagnostic and clinical consultant services in virology, infection medicine and antimicrobial stewardship for the University Medical Center.

**Projects**

**Tetraspanin Cd151 mediates particle morphogenesis of hepatitis**

- **Investigator:** Principal Investigator: Prof. Andreas Diefenbach
- **Duration:** Project duration: 2013 - 2018
- **Funding:** Eu FP7 245500
- **Sum:** € 1,500,000
- **Max. 5**

**Partikelmorphogenese des Hepatitis B-Virus:** Strategien, Mechanismen und Wirkungsfaktoren

- **Investigator:** Principal Investigator: Assoc Professor R. Prange
- **Duration:** Project duration: 2012 - 2015
- **Funding:** German Research Foundation (SFB 992)
- **Sum:** € 269,400
- **Max. 5**

**Active wound dressings based on biological mimicry**

- **Investigator:** Principal Investigator: Professor B Jansen
- **Duration:** Project duration: 2010 - 2014
- **Funding:** EU FP7 245500
- **Sum:** € 363,200
- **Max. 5**
II. Cell and Redox Signaling

ROS as a signal transmission mechanism are involved in inflammation, development, defense of bacteria and pathways govern the balance between survival and cell death. There is a delicate balance between ROS-producing enzymes (e.g. NADPH oxidases) and antioxidant enzymes (e.g. paraoxonases). Dysregulation of ROS production is intimately linked to human diseases (heart diseases, cancer).

The paraxoxasmes PON2/3 are the focus of our research. We analyze their regulation, mechanism and function in vitro and in vivo. PON2 has two independent functions: (1) reduction of mitochondrial ROS and enhancement of stress tolerance (important for cardiovascular diseases and cancer). (2) PON2 inactivates specific bacterial virulence factors. We want to understand the role of PONs in cardiovascular diseases (coagulation; atherosclerosis), cancer (angiogenesis; stress signaling) and acute bacterial infections.

III. Molecular Pharmacology/Immunopharmacology

Regulation of pro-inflammatory genes

Chronic inflammatory diseases are characterized by the overexpression of pro-inflammatory genes (cytokines, chemokines, inflammatory enzymes like the iNOS). The expression of pro-inflammatory genes is regulated both on the level of transcription and by post-transcriptional mechanisms (mRNA stability, -translation and localization). We analyze the DNA and RNA sequences and the protein factors important for the regulation of the human pro-inflammatory gene expression.

Regulation of pro- and anti-inflammatory genes: To protect cells against ROS the expression of anti-oxidative proteins is enhanced. We analyze which cis and trans-acting factors are important for the regulation of the expression of anti-oxidative proteins in human cells.

IV. Clinical Pharmacology and Pharmacogenetics

The sex-specific differences in the expression and activity of CYP3A: The CYP3A enzymes are central for the metabolism of drugs and toxins due to their abundance in the liver and gut and their wide substrate specificity. Dysregulation of CYP3A activity by activated SIRT1 and FOXO transcription factors.

Fig. 54: Regulation of human iNOS expression and activity

Fig. 55: Reduced NO bioavailability in atherosclerosis

The mechanism of the cardioprotective drug dexrazoxane.

V. Solute transport through biological membranes

Membrane transporter proteins mediate the transport of hydrophilic, charged and bulky molecules across the membrane of cells. Different human diseases (e.g. cystinosis, cystic fibrosis) are caused by the dysfunction or absence of these transporters. The topics of our current research are:

1) Expression, regulation and structure of cystic acid amino transporters (CATs)
2) Identification and characterization of the lysosomal transporter involved in cysteamine-mediated cystine efflux
3) Mechanisms of intracellular accumulation of the NOS inhibitor asymmetrical L-Arginine
4) Synthesis, radiosynthesis and evaluation of dimeric amino acid chelator complexes for tumor diagnostic and PET
5) Regulation and role of arginine transport in human T-Lymphocytes

VI. Gender-specific Medicine

Women have a higher probability to develop autoimmune, pro-inflammatory diseasess like rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). The molecular mechanisms causing this gender-specific dimorphism are not known. Beside genetic predisposition female sexual hormones may play a role in the enhanced disease rate in women. The groups analyze the gender-specific differences in the expression of pro- and anti-inflammatory gene involved in the pathogenesis of RA and SLE in cellular and animal models. In addition the molecular mechanisms leading to the enhanced cardiovascular mortality in RA and SLE patients is a focus of the current research.

Institutes of Clinical and Theoretical Medicine

IMPORTANT PROJECTS | MAX. 5

1. Expression, regulation and structure of cystic acid amino transporters (CATs)
2) Identification and characterization of the lysosomal transporter involved in cysteamine-mediated cystine efflux
3) Mechanisms of intracellular accumulation of the NOS inhibitor asymmetrical L-Arginine
4) Synthesis, radiosynthesis and evaluation of dimeric amino acid chelator complexes for tumor diagnostic and PET
5) Regulation and role of arginine transport in human T-Lymphocytes

Further: Healthcare and Social Research (Cooperation: Prof. H. Kleinert, Dr. S. Deng)

Fig. 53: Threedimensional analysis of the ex vivo angiogenesis of mouse aorta
The Institute of Legal Medicine is the stand alone University Forensic Institution in Rheinland-Palatinate and provides the complete forensic medical spectrum in research, education, and service.

To investigate the cause of death, the manner of death, and the identity of corpses as well as to reconstruct the accidental, homicidal, and suicidal flow of action, the forensic physicians perform more than 500 autopsies mandated by the prosecutor and some more mandated by insurances or by the relatives.

The Forensic Outpatient Unit provides the forensic clinical investigation and co-investigation of more than 700 living persons (adults and children), concerning the documentation and forensic appraisement of injuries and information of actions or accidents in cases of traffic accidents, conflicts between persons, neglect, and sexual offences. The Unit provides also expert opinions on the biological age of persons to differentiate between forensic relevant age limits. Those investigations usually need close cooperation with other clinical medical units, e.g. Radiology, Odontology, Pediatrics, Psychiatry, and Surgery. This field of Forensic Medicine (Clinical Forensic Medicine) is more and more developing in the last 10 years, though not as familiar to all possible clients as the field of Forensic Pathology. The service is increasingly requested not only by the investigative authority, but also by the clinical colleagues, the Youth Welfare Offices, and private persons (service for anonymous documentation and securing of evidence). The Forensic Outpatient Unit is financially supported by the Ministry of Internal Affairs, Sport, and Infrastructure independent from the budget for education and research by the Ministry of Education, Science, Qualification, and Culture.

To complete the service aspects, the Institute of Legal Medicine provides a department for Molecular Genetics on the fields of paternity testing, investigation of biological traces of evidence, clinical control of chimerism after bone marrow or stem-cell transplantation and a department of Forensic Toxicology for toxicology analyses of body fluids from living persons on the fields of drunken driving, driving under the influence of drugs, criminal responsibility in other criminal cases, and personal ability for driving. Both departments of the Institute of Legal Medicine also participate in the investigation of corpses (cause of death, identification).

The most important duty for the Institute of Legal Medicine as Part of the University Medical Center Mainz and the Johannes Gutenberg-University is the education of the students of Medicine and their training in the fields of future duties in the investigation of deceased persons according to the legal regulations and legal medical aspects, e.g. medical confidentiality, patient information for the informed consent, duty of emergency assistance, and proving of the ability for driving. Beside this, we provide lessons also for students of Biology and of course Law, and training courses for the police, lawyers, and medical assistant professionals.

The research is first and foremost applied research derived from questions arising in preparing expert opinions, partly also triggered by changes in legal regulations. The main topics in research are the following, mostly in cooperation with clinical colleagues:

- Analytical Method validation in Forensic Toxicology.
- Donor-/Acceptor-Chimerism Research after T-cell depleted allogenic stem-cell transplantation and administration of CD8-deleted donor-lymphocytes.
- Investigation of post-mortem re-distribution processes of drugs.
- Method validation of screening tests for drug detection in sweat and oral fluid.
- Investigations on the ossification of the medial epiphysis of clavicle for the estimation of the biological age of persons with different imaging procedures.
- Advanced GC-/LC-MS-search- and analysis-programs for so called knock-out drugs and the explosive increasing numbers of synthetic-chemicals.
- Epidemiology and possibilities for prevention of child maltreatment and sexual abuse.

**Important Projects**

**Fig. 56:** Dissecting Room

**Fig. 57:** Toxicology

**Anatomy in practise.**

Project Manager: Prof. T. Rasparth

Cooperation: Dr. I. Spiwoks-Becker, Institute of Microscopic Anatomy and Neurobiology

Funding: MAICUM

Sum: € 35,000

Project Duration: 2011—2013

**Population genetics of ADH and ADH variants in five Asian populations.**

Project Manager: Dr. K. Bender

Cooperation: Prof. H. Maida, University of Osaka Japan; Dr. D. Kim, University of Ho Chi Minh-City Vietnam

Funding: B.A.D.S.

Sum: € 5,000

Project Duration: 2013—2015

**Change of cerebral glucose metabolism activity in rats after THC-administration by PET-CT.**

Project Manager: Prof. R. Urban

Cooperation: Dr. I. Miederer, Department of Nuclear Medicine

Funding: B.A.D.S.

Sum: € 2,000

Project Duration: 2013—2015

**Post mortem computer tomography (PMCT) and CT-Angiography (PMCTA).**

Project Manager: Prof. D. Breitenauer

Cooperation: Dr. S. Hanus, St. Marien Hospital Ludwigshafen

Project Duration: 2013—2016
The Institute of Toxicology is one of the research institutes in Germany working on DNA damage and repair, DNA damage-triggered signaling and mechanisms of DNA damage-induced mutations, chromosomal changes, malignant transformation and cell death. Research is focused not only on chemical carcinogens, but also on ionizing radiation and ultraviolet light-induced DNA damaging insults. The main goal of our research is to gain a better understanding of the mechanisms that protect cells and organisms, including humans, against environmental and endogenously formed carcinogens on the one hand, and exploring the mechanisms of anticancer drugs aimed at improving cancer chemotherapy, on the other. The department hosts 8 working groups whose projects are tightly intertwined. Special emphasis is on brain and skin cancer (melanomas) that are treated with alkylating drugs. The department gains support from the German Research Foundation (DFG), German Cancer Aid (Krebsforschung) and Federal Ministry of Education and Research (MBF) with projects embedded in a radiation biology consortium (SISMEP).

1. Regulation of DNA repair
Here we explore genes and DNA repair functions that are upregulated following genotoxic stress. This research field is highly topical as it relates to the question of the existence of mechanisms for adaptation against harmful genotoxic exposures (tobacco smoke, poisons in food and beverages among others). In this context we also study the question of the existence of thresholds for chemical carcinogens.

2. DNA repair in the hematopoietic systems
We discovered that human monocytes express a very low amount of repair enzymes (XRCC1, PARP1 and others), which become upregulated during the differentiation of monocytes into macrophages and dendritic cells. Continuing this work, we have explored the mechanism of regulation of DNA repair in blood stem cells, in precursors of monocytic cells and their descendants. Upregulation of DNA repair protects macrophages and dendritic cells against reactive oxygen species and chemical carcinogens. We are also engaged in studies comparing the sensitivity of different blood cell populations to ionizing radiation and anticancer drugs. Our studies comparing the sensitivity of different DNA damage-induced breaks play a central role in cell death following alkylating agent treatment and DNA repair and protection against genotoxic stress. Furthermore, we analyze specifically the roles of HDACs and their inhibitors in tumor cells that are exposed to replicative and genotoxic stress.

3. DNA damage-induced signaling and apoptosis
In this project we focus on how specific DNA lesions in human healthy and cancer cells elicit signaling to downstream death mechanisms. The basic aim is to protect normal tissue while killing cancer tissue during therapy with genotoxic chemotherapeutics. Most genotoxicants, be they chemotherapeutic or environmental, cause modifications to DNA that have to be rectified or compensated for in order for the cell to survive. During the repair of these lesions, or in the absence of repair, deleterious DNA structures such as DNA double-strand breaks or stalled replication forks form that are detected by signaling kinases. We have established a method for activating these signaling pathways in blood stem cells in vitro, and by this evidence of its link to survival and death executed by apoptosis and other forms of cell death.

4. DNA damage-induced survival mechanisms
DNA repair and autophagy are key survival mechanisms following DNA damage. Autophagy is a catabolic process employed by the cell to remove damaged and unnecessary cellular components such as proteins and organelles and recycling them for the benefit of the cell. DNA damage-dependent activation of cell survival is controlled by autophagy. This stimulation of autophagy protects glioblastoma cells from chemotherapy-induced apoptosis.

5. DNA repair in the protection against colon cancer
In this project we focus on the protective role of DNA repair in colorectal cancer induced by alkylating Nitrosouro compounds (NOC). We use the azoxymethane-dextran sodium sulfate mouse model of colorectal carcinogenesis, monitoring tumor formation by non-invasive mini-endoscopy. Using transgenic DNA repair deficient mice, we analyzed the alkylation-induced DNA damage response in colorectal tumor cell lines, which is correlated with the dose-response of colorectal cancer formation. Another key aspect of our work is the sensitization of (colorectal) tumor cells by various strategies, e.g. by inhibition of DNA repair or by cellular delivery of apoptosis-inducing proteins. We are further interested in natural compounds, such as the dithiol-containing antioxidant lipic acid, and their impact on DNA repair and cell death pathways.

6. DNA repair in drug sensitivity of gliomas and malignant melanomas
For the treatment of malignant brain and skin cancer, alkylating agents are used. To reduce side effects and to enhance the killing response following treatment, an understanding of the regulation of these DNA-damaging chemotherapeutics is required. We have explored the mechanisms of these drugs and identified a) drug resistance mechanisms, b) drug sensitization of (colorectal) tumor cells by agents such as DNA double-strand breaks or stalled replication forks that are detected by signaling kinases. We have established a method for activating these signaling pathways in blood stem cells in vitro, and by this evidence of its link to survival and death executed by apoptosis and other forms of cell death.

7. Repair of crosslinks induced by chemotherapeutics
DNA interstrand crosslinks are induced by chloroethylating nitrosoureas (CNU’s) in a multistep process. Using different methods of downregulation (by siRNA) or pharmacological inhibition of HR proteins, we analyzed the effect on the cellular sensitivity of glioblastoma cells to these agents. We showed that HR in vitro and in a glioblastoma xenograft model is a key node in the cellular resistance to chemotherapy.

8. Mechanism of DSB formation
DNA double-strand breaks (DSBs) are ultimate trigger of cell death in radiation and chemotherapy of cancer. How do they arise? The paradigm that DSB arises following replication block provoked by DNA damage. In this project we demonstrated that a model DSB formation following MMS requires base excision repair (BER). Thus, BER has a Janus face: it removes damage from DNA on the one hand, and if this is not coordinated with replication, it may lead to replication errors resulting in DSB and chromosomal changes on the other.

9. Thresholds for genotoxic carcinogens
Chemicals that cause cancer by damaging and mutating DNA were once thought to be harmful at all doses. However, recent work has provided evidence that these chemicals may have a threshold dose-response. Here, a certain dose of chemical is needed before an increase in mutations is observed. Our research used a model DNA damaging alkylating agent to illustrate that DNA repair plays a protective role at low doses to prevent mutations. DNA damage is increased before the damage causes mutations thus giving a threshold dose-response. In cells defective in this repair, the protection is lost and all doses are damaging, thus giving the linear dose-response. This repair system (MGMT) significantly protects against tumor formation, but it is not able to completely prevent from it.

10. Stress-induced posttranslational modifications
Organisms modify their proteins and aberrant protein modifications are associated with severe diseases including cancer. This project focuses on proteins relevant for oncogenesis. We particularly address the regulation and physiological functions of acetylation, phosphorylation, and ubiquitylation. Furthermore, we analyze specific roles of HDACs and their inhibitors in tumors that are exposed to replicative and genotoxic stress.

The Institute of Toxicology
Department of Virology

**STRUCTURE, FUNCTION AND ORGANISATION OF THE DEPARTMENT**

Founded in 1994, the Institute of Virology represents the discipline Medical Virology in teaching and research with one C4 and one C3 professor, 2 group-leading staff scientists, and 3.5 positions for research technical assistants. Two consulting physicians with specialization for „Medical Microbiology, Virology, and Epidemiology of Infection“ supervise the medical service of virological laboratory diagnostics with 7 technical assistant positions for medical technical assistants. Focus of the medical service is on the molecular diagnostics of viral infections in immunocompromised patients, in particular in recipients of hematopoietic stem cell transplantation (HCT) as well as of viral infections in pregnancy.

Research at the institute flanks the focus areas of the medical service by specialisation on Cytomegalovirus (CMV) infections in immunocompromised HCT patients and corresponding mouse models. As CMV infection does not cause overt clinical symptoms in immunocompetent persons, there is little public awareness of CMV in Germany, unlike in the United States where CMV infection of the fetus is recognized as the major viral cause of birth defects with a significant impact on the health system giving high priority to developing a vaccine for protecting adolescent women. In addition, CMV infection is a major complication in the therapy of hematopoietic malignancies by HCT in that it causes graft failure and life-threatening interstitial pneumonia.

**MAIN FOCUS OF RESEARCH**

CMV belongs to the beta-subfamily of the herpesvirus family. Key features of CMV infection are successful immune control in the immunocompetent, healthy host that prevents disease and terminates productive infection, leading to a state of maintenance of viral genome in absence of virus production, a state known as “Latency”. Clinical problems arise when such latent viral genomes reactivate to productive infection under conditions of a weakened immune system.

The Institute of Virology is internationally renowned for basic research on the molecular virology and immunology of CMV infection as well as for translational research aimed at developing a CMV vaccine based on recombinant subviral particles. The scientific standing of CMV virology in Mainz is best documented by the fact that Prof. Reddehase (assisted by Dr. Lemmermann) served as the scientific editor of the most comprehensive science book ever published on CMV, entitled “Cytomegalovirus: From Molecular Pathogenesis to Intervention” (Caister Academic Press, 2 Vol., 2013).

The Institute of Virology is part of the priority research field “Immunology” of the University Medical Center. Research groups at the institute were funded by the German Research Foundation (DFG) in GRK 1043 and in the clinical research group KFO183, closely cooperating with colleagues at the Department of Hematology, Pneumology, and Oncology.

**Specific research projects:**

**GRK 1043, TP B3: Optimization of a subviral particle vaccine against human CMV infection**

Aims at the development of a particulate vaccine, based on subviral Dense Bodies (DBs). Recent experiments focused on the interaction of DBs with professional antigen-presenting cells and on the interference of human CMV with MHC class I mediated antigen presentation. Knowledge of these processes is essential for the rational design of a vaccine against human CMV.

**KFO183, TP B8: Establishing a challenge model for optimizing CMV-specific immunotherapy**

Aims at developing novel strategies for CMV therapeutic vaccination of HCT recipients based on human CMV Dense Bodies (DBs). Antigenicity-optimized, recombinant DBs will be evaluated for their protection-inducing capacity in a murine model of CMV infection with recombinant murine CMVs.

Development of an amniocyte cell culture system for human CMV propagation and vaccine production

In collaboration with CaP-CMV GmbH, Cologne, this translational project deals with the establishment of a cell culture for the large-scale production of DBs. For this, the amniotic cap-cell line is being evaluated to induce a significant increase in the percentage of CMV Tregs, whereas CD4 Tregs were barely affected. This finding points to an unexpected relevance of CD4 Tregs for murine CMV-immune control. This project will be part of an SFB proposal.

Pathophysiologic interaction between chronic murine CMV infection and allergic airway disease.

**Immune control of murine CMV infection after deletion of immunodominant CD8 T-cell epitopes**

Functional deletion of all immunodominant CD8 T-cell epitopes of murine CMV, as defined by the quantity of the response, revealed that the corresponding CD8 T-cell specificities are dispensable and that subdominant specificities, raising high-avidity CD8 T cells, suffice for control of murine CMV infection. This finding has implications for the antigen composition of vaccines.

Influence of regulatory T cells (Tregs) on the immune control of murine CMV infection.

Remarkably, murine CMV infection proved to induce a significant increase in the percentage of CD4 Tregs, whereas CD4 Tregs were barely affected. This finding points to an unexpected relevance of CD4 Tregs for murine CMV-immune control. This project will be part of an SFB proposal.

Pathophysiologic interaction between chronic murine CMV infection and allergic airway disease.

**Preliminary data provide first indication for a synergy between murine CMV and allergic airway disease. Both entities induce an enhanced immunological reaction in a mutual manner. Murine CMV promotes an OVA-specific CD8 T-cell response, and OVA administration enhances the murine CMV peptide specific CD8 T-cell response.**

**IMPORTANT PROJECTS | MAX. 5**

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Project Manager</th>
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<tr>
<td>Development of an amniocyte cell culture system for human CMV propagation and vaccine production</td>
<td>Prof. B. Plachter</td>
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<td>2011 - 2014</td>
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<tr>
<td>Establishing a challenge model for optimizing CMV-specific immunotherapy</td>
<td>Prof. B. Plachter, Prof. M. Reddehase</td>
<td>Dr. RH Voss, Department of Hematology, Pneumology, and Oncology, Prof. M. Marschall, Institute of Clinical and Molecular Biology University of Erlangen, Prof. Ch. Sinzinger, Institute of Virology University of Tübingen et al.</td>
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**Development of an amniocyte cell culture system for human CMV propagation and vaccine production**

**Project Manager:** Prof. B. Plachter

**Cooperation:** Fa. CAP-CMV GmbH Cologne

**Funding:** CAP-CMV GmbH Köln

**Project Duration:** 2011 - 2014

**Establishing a challenge model for optimizing CMV-specific immunotherapy**

**Project Manager:** Prof. B. Plachter, Prof. M. Reddehase

**Cooperation:** Dr. RH Voss, Department of Hematology, Pneumology, and Oncology, Prof. M. Marschall, Institute of Clinical and Molecular Biology University of Erlangen, Prof. Ch. Sinzinger, Institute of Virology University of Tübingen et al.

**Funding:** German Research Foundation

**Project Duration:** € 1,248,400

**Project Duration:** 2007 - 2013

**Optimization of a subviral particle vaccine against human CMV infection**

**Project Manager:** Prof. B. Plachter

**Cooperation:** Prof. M. Marschall, Institute of Clinical and Molecular Biology University of Erlangen, Prof. W. Hart, Department of Hematology, Pneumology, and Oncology, Dr. U. Hartwig, Department of Hematology, Pneumology, and Oncology et al.

**Funding:** German Research Foundation

**Project Duration:** € 135,900

**Project Duration:** 2009 - 2013
The TIM has been founded with the appointment of Prof. D. Schuppan at UMC Mainz. It is a unique institute aiming at bringing diagnostic and therapeutic developments from bench to bedside. It maintains strong links with Harvard Medical School (HMS) in Boston. Unique clinical activities are focused on small intestinal inflammatory diseases, including celiac disease, and novel food intolerances. Other diseases are addressed clinically in collaborations, e.g., fatty liver disease, liver fibrosis, liver cancer and similar diseases affecting other organs such as the skin, both with other departments at UMC Mainz and at HMS. As an example, the TIM runs the only specialized clinic for complicated celiac disease, wheat sensitivity and associated autoimmunity nationwide. The TIM is embedded in the Research Center of Immunotherapy (FZI) at UMC Mainz which bundles the immunological expertise of the 4 immunological institutes and the clinical and basic departments with a focus on immune mediated diseases including cancer. This entails strong links with the Institute of Translational Oncology, the Research Center for Translational Neurology, and cooperative projects with the basic research institutes on the university campus, especially chemistry, the MPI for polymer chemistry and Nuclear Chemistry, resulting in numerous joint translational research projects, some of which have lead to projects within collaborative research initiatives (SFBs), EU projects or others. Apart from these clinical and research activities, the TIM is active in lecturing in (translational) medicine and basic research, and guiding, promoting and mentoring Master’s, MD and PhD students in Translational Immunology/Medicine within the above mentioned networks. The staff of the TIM is >80% international and >90% is funded via competitive research grants or fellowships.

1. The molecular and cell biology of chronic liver diseases. Explanation of the cellular, molecular and signaling mechanisms of excess scar tissue deposition in fibrosis and cirrhosis and mechanisms of its dissolution (fibrrosis). These studies are linked to translational projects that are aimed at 1. developing non-invasive techniques for monitoring fibrogenesis and fibrosis in rodents and patients (devising and exploring quantitative imaging agents and novel protein and microparticle markers in serum and plasma), 2. characterization and validation of several potential antifibrotic and fibrosis reversal-inducing molecules and cellular therapies. Here, human and experimental in vitro and vivo models of liver fibrosis, inflammation, and oxidative stress are exploited, such as primary and secondary biliary fibrosis, lobular fibrosis and especially non-alcoholic steatohepatitis (NASH), including novel predictive mouse models for primary liver cancer and liver and lung metastasis. Future studies are performed with activated hepatic stellate cells, myofibroblasts, Kupffer cells/macrophages, dendritic and myeloid precursors, lymphocytes, progenitor and mast cells. Specific projects explore modulation of hepatic progenitor/oval cells and macrophages to induce fibrosis reversal and cancer regression. Moreover, the collaboration with immunology groups, organ and cell specific nanoparticles for effective delivery of small molecules and siRNA are evaluated. Finally, the group works on mouse models with humanized mice, e.g. myelofibrotic, specific inducible promoters for the knockdown of potential fibrosis- or immune-system-relevant genes, or transgenic mice for the study of cancer related mechanisms and therapies.

2. The molecular pathogenesis and immunology of chronic intestinal diseases, including celiac disease. Prior and current research has lead to the identification of the celiac disease autoantigen, tissue transglutaminase (TG2), and focused on exploring the role of TG2 in celiac disease pathogenesis, including the clinical development of a TG2 inhibitor as novel treatment for celiac disease within the CI3 excellence cluster. As one of the beacon projects “KETI-Clinical development of transglutaminase-inhibitors for treating celiac disease” is financed jointly by the Federal Ministry for Education and Research and the European Regional Development Fund (ERDF) with a total sum of 489,010.80 for UMC Mainz until June, 30 2015. Further funding depends on the success of an ongoing phase 1 clinical study. The CI3 cluster’s strong networking capability is reflected in research and development projects in which partners of the cluster region collaborate in the field of individualized immune intervention. Several approaches are undertaken to develop a mouse model for celiac disease, including mice with a humanized immune system, to allow the preclinical testing of non-dietary and immune modulatory therapies. We have recently identified amylose trypsin inhibitors (ATIs) of wheat/barley/rye as triggers of nonceliac/non-allergy wheat sensitivity that after oral ingestion uniquely activate intestinal myeloid cells via toll like receptor 4 to cause low level intestinal immune stimulation. How far nutritional ATIs promote intestinal and extraintestinal inflammatory diseases is subject of numerous current preclinical and imminent clinical studies. We also search for serum activity markers of celiac disease and wheat sensitivity. A growing group in the lab studies the myeloid cells and their modulation in inflammatory bowel diseases, including the search for novel biomarkers of disease activity.

3. The role of macronutrients and the microbiota in intestinal and extraintestinal inflammatory diseases. This has become a recent research focus. Major emphasis is on common carbohydrates, ATIs in gluten containing cereals, and major lipids, their interaction with the intestinal microbiota and the immune system. Major diseases assessed in rodent models and planned clinical studies are IBD (IBS), NASH/type 2 diabetes, and cardiovascular disorders.

4. The role and modulation of innate immunity in cancer. Several projects investigate and target the myeloid suppressor cells in various cancers, including metastatic melanoma and primary liver cancer. These studies are interconnected with the projects studying adaptive immunity in cancer within the above institutions.

5. Collaborative research. The above initiatives are not limited to gastrointestinal and liver diseases but are increasingly generating synergies with other clinical departments, such as dermatology (melanoma, scleroderma, food sensitivities and skin disorders), cardiology (metabolic syndrome/NASH and cardiovascular pathology), neurology (e.g., ATIs and autoimmune neurological disease like multiple sclerosis), or hematology/oncology.

The Institute of Translational Immunology (TIM)

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M A I N F O C U S O F R E S E A R C H

1. Developing non-invasive techniques for monitoring fibrogenesis and fibrosis in rodents and patients (devising and exploring quantitative imaging agents and novel protein and microparticle markers in serum and plasma).
2. Characterization and validation of several potential antifibrotic and fibrosis reversal-inducing molecules and cellular therapies.
3. Exploring the role of tissue transglutaminase (TG2) and other celiac disease autoantigens in celiac disease pathogenesis.
4. Developing a mouse model for celiac disease.
5. Investigating the interaction of nutrition and the microbiota with intestinal and extraintestinal inflammatory diseases.

IMPORTANT PROJECTS | MAX. 5

Development of Serum Markers for the Assessment of Liver Fibrosis Progression and Reversal
Project Manager: Prof. D. Schuppan
Funding: Foundation of the State Rhineland-Palatinate
Sum: € 249,259
Project Duration: 2013 - 2015

Evaluation of the anti-fibrotic effect of three anti-fibrotic compounds in experimental biliary and panniculotubular liver fibrosis
Project Manager: Prof. D. Schuppan
Funding: Boehringer Ingelheim International GmbH
Sum: € 151,350
Project Duration: 2013 - 2015

Mechanistic and therapeutic studies for nonalcoholic steatohepatitis (NASH)
Project Manager: Prof. D. Schuppan
Funding: Boehringer Ingelheim International GmbH
Sum: € 150,000
Project Duration: 2012 - 2015

Quantitative Imaging of Liver Fibrosis and Fibrogenesis
Project Manager: Prof. D. Schuppan
Funding: EU
Sum: € 2,000,000
Project Duration: 2012 - 2017

Therapy of Metastatic Melanoma by Addressing Tolerance Inducing Macrophages
Project Manager: Prof. D. Schuppan
Funding: German Research Foundation
Sum: € 201,450
Project Duration: 2013 - 2013

Institutes of Clinical and Theoretical Medicine
Departments of Conservative Medicine

- Department of Dermatology
- Department of Medicine I
- Department of Medicine II (Cardiology, Angiology and Intensive Care)
- Department of Hematology, Pneumology, and Oncology
- Department of Psychiatry and Psychotherapy
- Department of Child and Adolescent Psychiatry and Psychotherapy
- Department of Neurology
- Department of Psychosomatic Medicine
- Center for Childhood and Adolescent Medicine (ZKJM)
Department of Dermatology

The Department of Dermatology is the only academic Dermatology department in Rheinland-Palatinate and one of the largest dermatology Hospitals of the Rhine-Main area. The Department has 45 beds on two wards for inpatient treatment of skin disorders and also offers a variety of outpatient clinics. Five professors, eight senior physicians and fifteen specialists and junior doctors ensure medical diagnostics and therapy on the highest level. We offer state of the art diagnostic equipment and therapy in all areas of dermatology. In addition to skin specialists, the Department has medical staff with special knowledge in allergy, occupational dermatology, medical tumor therapy, palliative care, diagnostic ultrasound, proctology, phlebology, plastic surgery, alternative medicine and medical quality management. In addition, the Department hosts a basic research laboratory with 50 researchers, and we also conduct >50 clinical trials on innovative therapies in dermatology in our Clinical Research Center (CRC, PD Dr. Staabach, Dr. Loquai), which acts as an interface between clinical basic and applied research.

MAIN FOCUS OF RESEARCH

Well characterized scientists with their employees investigate immunobiological causes of skin diseases and autoimmunity and allergy. The clinical research unit allergy (Prof. Reske-Kunz) examines immune cells, which are essential for symptoms of type I allergies and develops new strategies for targeted suppression of these mostly by antibodies induced diseases. Research for the development of allergic diseases, is also the focus of Prof. Saloga and PD Dr. Bellingshausen. How dendritic cells in interaction with T cells control immune response and prevent allergies, but simultaneously fight against infectious agents is the research focus of Prof. Steinbrink and Prof. Stiebut-Borschitz. The focus of the working group of HD Dr. Jonuleit is the study of the regulatory T cells, immune cells that prevent autoaggressive and allergic immune responses. The molecular characterization of T cell function and dysregulation and control the induction of type I allergy (Prof. Reske-Kunz, Prof. Saloga, PD Dr. Bellingshausen) is also the focus of Prof. Saloga and PD Dr. Bellingshausen. How dendritic cells in interaction with T cells control immune response and prevent allergies, but simultaneously fight against infectious agents is the research focus of Prof. Steinbrink and Prof. Stiebut-Borschitz. The focus of the working group of HD Dr. Jonuleit is the study of the regulatory T cells, immune cells that prevent autoaggressive and allergic immune responses. The molecular characterization of T cell function and dysregulation and control the induction of type I allergy (Prof. Reske-Kunz, Prof. Saloga, PD Dr. Bellingshausen) is also the focus of Prof. Saloga and PD Dr. Bellingshausen. New multifunctional polymers for immunotherapeutic treatment of melanoma (Prof. Grabbe, Prof. K. Steinbrink, HD Dr. Jonuleit, PD Dr. Becker, Prof. Reske-Kunz) and the investigation of dendritic cells in the development of protective immunity (Prof. Grabbe, Prof. Steinbrink, HD Dr. Jonuleit, Prof. Reske-Kunz) are the focus of the working group of Prof. von Stiebut-Borschitz.

Important projects:

1. Analysis and modulation of allergic immune responses in an established humanized mouse model
   Project Manager: PD Dr. I Bellingshausen
   Project Duration: 2012 - 2013
   Project Manager: PD Dr. H Jonuleit
   Cooperation: Prof. H Wiendl, University hospital Münster

2. Analysis and therapeutic modification of T cell responses in multiple sclerosis
   Project Manager: PD Dr. H Jonuleit
   Project Duration: 2012 - 2016

3. Development and testing of nanoparticle for inhibition of cAMP-mediated immunosuppression of malignant melanoma
   Project Manager: Prof. T Bopp

4. Mast-cells - promoters of health and modifiers of disease
   Project Manager: Prof. Re von Stiebut
   Funding: German Research Foundation Sum: € 465,150
   Project Duration: 2012 - 2015

5. Polymer-mediated in situ activation of dendritic cells for tumor immunotherap-iy
   Project Manager: Prof. H Schild, Prof. S Grabbe
   Funding: German Research Foundation Sum: € 414,700
   Project Duration: 2013 - 2017
Department of Medicine I

Director: Professor Peter R. Galle

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IMPORTANT PUBLICATIONS | MAX. 5


Marquardt JU, Fischler K, Baus K et al. Sirtuin-6-Dependent Genetic and epigenetic Alterations Are Associated With Poor Clinical Outcome in Hepatocellular Carcinoma Patients. HEPATOLOGY. 2013; 58 (3): 1054–1064.


STRUCTURE, FUNCTION AND ORGANIZATION OF THE DEPARTMENT

The I. Department of Internal Medicine has an outstanding international reputation and provides patient care on a wide range of internal diseases. In 2013, in 100 beds (incl. 11 ICU beds) 4,896 admissions were handled, 1,678 cases partial inpatient and 17,647 cases (= 41,160 visits) outpatient treatments.

MAIN FOCUS OF RESEARCH

Gastroenterology
The clinical and scientific focus is on diagnosis and treatment of diseases of the gastrointestinal tract of the body, including the esophagus, stomach, intestines, liver, gallbladder, pancreas, color, and rectum. Special emphasis is given to chronic inflammatory bowel disease.

Gastroenterological Endoscopy / Ultrasound Sonography
At the core of gastroenterological diagnostics are endoscopic and ultrasonographic examinations of the stomach, intestine and bile ducts. The Department of Medicine I has a large unit in all standard endoscopic procedures as well as a number of specialized and innovative procedures that were developed in Mainz are performed.

Gastroenterological Oncology
Care of patients with all tumors of the digestive tract such as colon and stomach cancer, and, as a special focus, hepatocellular carcinoma.

Hepatology
The clinical focus spans the field of hepatology including viral hepatitis, liver tumors, autoimmune diseases, cholestatic diseases, fatty liver disease, fibrotic diseases, and all aspects of liver transplantation. The basic research focuses on the regulation and function of genes that play a central role in the onset of liver diseases. The understanding of the complex interaction of these molecules is of great clinical importance for the development of new therapeutic strategies.

Nephrology
Comprehensive care of patients with all forms of acute and chronic kidney disease and hypertension including patients with immunologically mediated diseases with renal involvement (i.e. vasculitis). Furthermore, we perform bone biopsies to guide treatment of renal osteoporosis. Treatment of end stage kidney disease and preparation of patients for dialysis initiation including dialysis access surgery in cooperation with the section of vascular surgery is performed at our division, hemodialysis/peritoneal dialysis, and kidney transplantation. Apart from hemodialysis we perform also all forms of extracorporeal treatment procedures including plasma separation, immunoadsorption, liver support, and lipid apheresis. A special focus of the division is kidney transplantation including living donor / (EO1) ABO incompatible (LABO) kidney transplantation.

Intensive Care Unit
All patients with acute organ dysfunction requiring intensive care. A focus lies on acute and complex chronic renal and liver failure.

Infectiology
Infectious diseases, including tropical diseases, Hepatitis B and C, HIV-infection and AIDS.

Rheumatology
Diagnosis and management of the entire spectrum of rheumatic and musculoskeletal diseases.

Endocrinology
Services for inpatient and outpatient treatment of all endocrine and metabolic disorders are offered. The spectrum includes diabetes mellitus and its complications such as diabetic foot ulcers, disorders of the pituitary gland, the thyroid and parathyroid, adrenal gland, and the sex hormones. Further focus are osteoporosis and dyslipidemia, diagnosis and treatment of endocrine and neuroendocrine tumors and nutritional medicine.

IMPORTANT PROJECTS | MAX. 5

Core-Facility: Imaging Center
Project Manager: Dr. D Strand
Sum: € 270,000
Project Duration: 2012 - 2014

Mechanisms of circadian clock gene regulation by Birc6 in hepatocytes
Project Manager: Prof. S Strand
Cooperation: Prof. S Thorgeirsson, Laboratory of Experimental Carcinogenesis, Bethesda USA
Funding: Boehringer Ingelheim Foundation
GRK Dynamics of Gene Regulation, Epigenetics and DNA Damage Response
Sum: € 54,000
Project Duration: 2012 - 2015

Pharmacogenomic-based targeting of Cancer Stem Cells in hepatocellular cancers: implications for relapse formation
Project Manager: Dr. JU Marquardt
Cooperation: Dr. S Thorgeirsson, National Cancer Institute Bethesda
Funding: German Cancer Aid
Sum: € 197,208
Project Duration: 2013 - 2016

Role of the proto-oncogene bcl-3 during initiation and progression of hepatocellular carcinoma (HCC)
Project Münster: Prof. Dr. M Wörns, PD Dr. J Schattenberg
Cooperation: Prof. A Wasiman, Institute of Molecular Medicine
Funding: German Cancer Aid
Sum: € 244,000
Project Duration: 2013 - 2016

Role of the proto-oncogene Bcl-3 during initiation and progression of hepatocellular carcinoma (HCC)
Project Münster: PD Dr. JM Schattenberg, PD Dr. M Wörns
Cooperation: Prof. A Wasiman, Institute of Molecular Medicine, Prof. D Schuppan, Institute of Translational Medicine, Mark Czaja MD, Einstein College of Medicine, New York
Funding: German Cancer Aid
Sum: € 244,303
Project Duration: 2013 - 2016
Department of Medicine II (Cardiology, Angiology and Intensive Care)

STRUCTURE, FUNCTION AND ORGANIZATION OF THE DEPARTMENT

The Department of Medicine II is one of the leading cardiology centers in Rheinland-Palatinate and the metropolitan Rhine-Main area. The clinic has 78 beds on three wards, of which 24 beds can be monitored. In addition, it has an internal medicine intensive care unit with a total of 20 beds (12 intensive and 8 intermediate care beds) and a Chest Pain Unit with 10 monitored beds. The clinic also has the organizational responsibility for the emergency department. The main focuses of the clinic are treatment of patients with acute coronary syndromes (ACS) and chronic stable coronary artery disease, interventional valve therapy including transcatheter aortic valve implantation (TAVI), mitral valve clipping and interventional electrophysiology including ablation of paroxysmal and persistent atrial fibrillation. Newly introduced procedures include the interventional occlusion of arterial septum and the ablation of the renal arteries. The offer is complemented by special consultations in the field of heart failure, pulmonary hypertensive heart disease, arrhythmias and cardiovascular prevention. Other major diagnostic areas include echocardiography and angiography. In 2013, the clinic treated about 9,000 inpatients and about 16,000 outpatients. The clinic has three modern cardiac catheterization laboratories in which per year 4,000 diagnostic cardiac catheterizations and 1,800 percutaneous coronary interventions are performed in patients with stable coronary heart disease, acute myocardial infarction, heart failure and valvular disease and arrhythmias. Furthermore, we implant approximately 270 pacemakers and 150 defibrillators with or without resynchronization. Our Chest Pain Unit, one of the first being established in Germany in 2005, treats more than 4,000 patients with Chest Pain and suspected myocardial infarction. We also have an excellent heart network with cardiologists and clinics within Rheinland-Palatinate. In the 2013 our clinical study center was involved in more than 30 clinical trials. About 350 patients were enrolled in ongoing clinical trials and more than 450 patients could be included in new clinical trials within the last year. The recently published FOCUS ranking places us at position 11 of all cardiology departments in Germany. Our aim is of course to get listed among the best ten next year.

MAIN FOCUS OF RESEARCH

The key research areas of the Department focus on the identification of causes leading to vascular damage. In preclinical and clinical studies we investigate the influence of genes and traditional risk factors and the diagnostic value of biomarkers with respect to cardiovascular disease. In particular, we explore these relationships in the Gutenberg Health Study, one of the largest prospective cohort trials worldwide. Furthermore, we focus on the mechanisms of improvement of vascular damage by drug therapy. The Department of Medicine II is part of the successfully established Centre of Thrombosis and Hemostasis (CITH) and also of the German Center for Cardiovascular Research (DZHK). Recent findings established the role of inflammatory cells in causing vascular damage and arterial hypertension (Philip Wenzel, Sabine Kossmann, Maike Knorr). New antiinflammatics such as the glitazones (DP4-4) inhibitors were characterized to have potent anti-inflammatory and vascular protective properties not only in the setting of diabetes mellitus but also in aripathy. The research group led by Katrin Schaffer (Translational Vascular Biology) investigates the role of specific factors expressed in perivascular adipose tissue in causing atherosclerosis. The translation role of the preclinical results was achieved by using endothelial function measurements such as flow dependent dilatation and constiction e.g. in patients with a coronary heart disease and peripheral arterial occlusive disease (Tommaso Gori (Translational Vascular Medicine); Christine Esprinta-Riehen (Angiology)). In 2012 the Gutenberg Health Study (GHS) successfully finished the recruitment phase by including 15,010 participants (Philip Wild, Thomas Münzel), and the follow-up examination for the next five years is under way. The research program of the GHS includes a new vascular examination station for leg veins, sonography of the abdominal aorta and femoral arteries. In Mainz, we established Europe’s largest biobank for cardiovascular and cerebrovascular late sequelae in long-term survivors of childhood cancer (Karin Merz). The team conducting a clinical trial investigating the role of specific factors expressed in perivascular adipose tissue in causing atherosclerosis. The translation role of the preclinical results was achieved by using endothelial function measurements such as flow dependent dilatation and constiction e.g. in patients with a coronary heart disease and peripheral arterial occlusive disease (Tommaso Gori (Translational Vascular Medicine); Christine Esprinta-Riehen (Angiology)). 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Fig. 64: Preparing for Transcatheter Valve Implantation (TAVI)

Fig. 65: The team conducting a TAVI (Transcatheter Valve Implantation)
Department of Hematology, Pneumology, and Oncology

IMPORTANT PUBLICATIONS | MAX. 5


Hoss G, Meyer RG. Transplantation in follicular lymphoma: not "yes or no" but "whom and when?". HAEMATOLOGICA 2013; 98 (9): 1333-1334.


MAIN FOCUS OF RESEARCH

Clinical Research
Clinical research is key to the rational improvement of therapeutic options for patients. Our study section on hematology, oncology, infectious disease, hemostasiology, and palliative care (principal investigator (PI): Georg Hess) is responsible for the due comprehensive clinical trial management with an emphasis on early, phase I/II clinical trials. It provides 24-7 service and ensures that international ethics and scientific standards, laws and regulations (AMG, CH-GCP) are met. Our pneumology study section (PIs: Roland Buhr, Stephanie Korn) has an emphasis on airway disease and provides equivalent service.

Translational and Basic Research
The foci of translational and basic research within the department range from tumor immunology (PIs: Hakim Echchammas, Udo Hartwig, Markus Munder, Markus Radak, Matthias Theobald, Thomas Wolf), the immunobiology of stem cell transplantation (PI: Eva Wagner) and nanoparticles (PI: Vocker Mailänder), the immunobiology of airway disease (Pis: Roland Buhr, Sebastian Reuter), the molecular basis of malignant hemopoiesis (PI: T. Kindler) to translational research in hemostasiology (Pls: Charles von Auer, Inge Scharrer). The research laboratories and principal investigators are actively involved in due international, European, and national research programs, and are further part of due collaborative research programs and graduate schools in both, the University Medical Center and the Johannes Gutenberg-University Mainz.

Fig. 68: Prof. Matthias Theobald and team, ward round

Fig. 69: Production facility for cellular therapeutics

Fig. 67: Laboratory

IMPORTANT PROJECTS | MAX. 5

Engineering of T cell receptors (TCRs) for adoptive immunotherapy of hematologic malignancies
Funding Organization: German Consortium for Translational Cancer Research (DKTK), Federal Ministry of Education and Research
Funding Sum: € 120,000
Duration: 2013 - 2015

BERT – A phase I/II trial to evaluate the safety, feasibility and efficacy of the addition of Temsirolimus (Torisel) to a regimen of Bendamustine and Rituximab for the treatment of patients with follicular lymphoma or mantle cell lymphoma in first to third relapse
Funding Organization: Wyeth Pharma/Pfizer, Mundipharma, Prof. M Seibert-Grafe, Interdisciplinary Center for Clinical Studies Mainz German Low-Grade Lymphoma Study Group
Cooperations: Dr. C Medic, Interdisciplinary Center for Clinical Studies (IZK) Mainz
Funding Sum: € 318,150
Duration: 2009 - 2016

The impact of AML – stromal cell interaction on malignant transformati- on, maintenance of leukemic stem cells and drug resistance
Funding Organization: German Research Foundation
Funding Sum: € 297,000
Duration: 2010 – 2013

Interaction of nanoparticles with cellular compartments and proteins
Funding Organization: German Research Foundation
Funding Sum: € 252,500
Duration: 2008 - 2014

Regulation and role of arginine trans- port in human T-lymphocytes
Cooperation: Prof. B Cloos, Institute of Pharmacology, Mainz
Funding Organization: German Research Foundation
Funding Sum: € 199,825
Duration: 2012 - 2015
The Department of Psychiatry and Psychotherapy is among the largest departments of the University Medical Center of the Johannes Gutenberg University Mainz comprising 126 inpatient and 9 day hospital treatment places as well as a range of specialized outpatient clinics. The Department is the compulsory mental health institution for the city of Mainz providing the care for more than 200,000 people locally as well as specialized psychiatric services for the state of Rhinehain-Palantine, the Rhine-Main metropolitan area and other areas of Germany. Treatment for international patients is offered as well and is organized by the International Office of the University Medical Center. Special treatment units and wards are established for affective disorders (major depressive disorder, bipolar disorders), schizophrenia spectrum and other psychotic disorders, substance-relate and addictive disorders (especially alcohol addiction), disorders of elderly and orphan diseases (especially dementia and neurocognitive disorders), and Borderline Personality Disorder as well as other Personality Disorders and trauma-related disorders. Additionally, the Department also has a general intensive care locked ward and a general elective services ward for patients with private insurance. As part of the maximum care Medical Center the Department offers state-of-the-art extensive diagnostic and treatment options for the whole spectrum of psychiatric disorders in close collaboration with other departments by the use of cutting edge diagnostic equipment and techniques. Therapies are based on a multidimensional disease conceptualization and involve pharmacological, psychophar- macological, neuropsychological and psychosocial treatment methods. Highest standard of care is achieved by the implementation of Evidence Based Medicine (EBM) as well as national and international guidelines into routine treatment. In fact, the critical and scientifically guided evaluation of psychopharmacological and psychotherapeutical treatment options in the light of conflicts of interest is a nationally and internationally renowned characteristic of the Department and especially of its chairman. Honoring his engagement, Prof. Klaus Lieb has been awarded with the prestigious “Hochschulprofessor des Jahres” prize in 2013 for his outstanding achievements concerning clinicians’ vigilance toward conflicts of interest and strategies into patient-centered independent clinical care, education and research. In 2013, the Department has been certified according to the ISO 9001:2008 norm for its definition of standard operating procedures in all areas of clinical care.

IMPACTFUL PROJECTS

- The research focus "normal aging and pathological neurodegeneration" uses a wide spectrum of methods from biochemical and/or clinical approaches to mice to men (RET, MRT, DTI) to translationally understand the neuro-pathology of Alzheimer’s disease as well as the neurophysiology of normal aging and to develop new therapeutic strategies and substances which are immediately tested in clinical studies.

- The Chairman's team uses innovative attempts to investigate neuroscientific aspects of 'cognitive enhancement' by means of randomized controlled trials investigating the efficacy of putative cognitive enhancers, of different populations as well as several interdisciplinary research projects supported by the German Federal Ministry of Education and Research (BMBF).

- The research focus “Emotion Regulation and Impulse Control (ERIC)” uses a wide variety of functional imaging methods (fMRI, EEG, EGG, EEG-fMRI) and genetic information to characterize the neurobiological foundations of two cognitive functions - emotion regulation and impulse control - which are key for normal psychological functioning and are often altered in psychiatric disorders such as Attention Deficit Hyperactivity Disorder (ADHD) and Borderline Personality Disorder (BPD).

- Functional Psychiatry and Psychotherapy is the most recent addition to the Department. Aside from its main task providing forensic assessment for local and regional courts, Functional Psychiatry investigates the neurobiology of disorders often found to be associated with disruptive behaviors like ADHD in close collaboration with ERIC.

- Neuroethics

- The chairman’s team uses innovative attempts to investigate neuroscientific aspects of “cognitive enhancement” by means of randomized controlled trials investigating the efficacy of putative cognitive enhancers, of different populations as well as several interdisciplinary research projects supported by the German Federal Ministry of Education and Research (BMBF).
Department of Child and Adolescent Psychiatry and Psychotherapy

The Department of Child and Adolescent Psychiatry and Psychotherapy is the only university-based institution in Rhineland-Palatinate for this subject of study. It covers together with neighboring states the densely populated Rhine-Main area. The primary aim is a science and teaching oriented institution, continually developed since 2007 under the direction of Prof. Dipl.-Psych. Michael Huss. The department’s major research fields are in child and youth psychiatry with the additional link to psychiatry in adults (adult ADHD and Fragile-X-Syndrome).

With the first compulsive teaching model in medicine in Germany we transfer this knowledge with an innovative teaching concept. We secure maximum benefit for students by using interactive didactic, experience based lessons including treating of patients. The success is reflected by the constantly excellent student evaluations.

This close collaboration with the college dean resulted in a Mindfulness-based stress reduction program for medical and dental students that was established in 2012. A cooperation with the Rheinhausen-Fachklinik Mainz, Child and Adolescent Psychiatry, Psychotherapy and Psychosomatic, which is headed by Prof. Dipl.-Psych. Michael Huss, provides both outpatient treatment and inpatient treatment for 40 patients. Children and adolescents with all types of psychiatric disorders are being treated. A specialized outpatient clinic for Eating Disorders was founded in 2010 as a direct link between University Medicine in Mainz and standard healthcare provided by the Rheinhausen-Fachklinik.

The primary aim is a science and teaching oriented institution, continually developed since 2007 under the direction of Prof. Dipl.-Psych. Michael Huss.

MAIN FOCUS OF RESEARCH

- Key research areas include eating disorders (Anorexia Nervosa, Bulimia Nervosa, Binge Eating Disorder), ADHD (Attention-Deficit/Hyperactivity Disorder), depression and Fragile-X-Syndrome. Additionally, focal points of interest include primary prevention with healthy populations as adolescents (prevention of eating disorders) and medicine students (prevention of stress and stress related disorders).

Eating Disorders:

These disorders are serious illnesses due to frequent somatic comorbidity, high mortality rates and challenging treatments. "Therapeutic idealisation", pressure to be thin and the desire to lose weight has increased over the years and has been found as a major risk factor for eating disorders, possibly leading to eating disorders.

In this key research area we are establishing a corporate concept for analysing prevalence, primary prevention, treatment and additional groups for family members.

The Mini-step-project (Manzner Schulentwicklung für Essstörungsprävention) was started in cooperation with the insurance group KKH (Kaufmännische Krankenkasse), the Department of Social Issues, Employment, Health and Demography (MSAGD), the Department of Education, Science, Qualification and Culture (MBWK) and the Association for Facilitating Feminist Social Work for Girls (FEMMA) as well as the Regional Association for Family Members of Mentally Disordered Rhineland-Palatinate. We established the school based, evaluated primary prevention program in 20 schools in 2013 and designed an additional secondary prevention program. Concepts based on Cognitive-Behavioural and Dialectical Behavioural strategies were developed and introduced for the treatment of apparent eating disorders and education and skills training for family members.

ADHD:

Attention-Deficit/Hyperactivity-Disorder is one of the most prevalent mental disorder in children and adolescents. Patients exhibit attention deficits, hyperactivity and impulsivity with functional impairments in daily activities. Primary issues of interest include treatment procedures (pharmacological and supplement based) and measurements of adherence in pharmacological treatment. The FAD study seeks to analyse treatment outcomes with polysaturated fatty acids like fish oils whereas the Guanfacine study targets a drug, initially prescribed for the treatment of high blood pressure in adults, in the treatment of ADHD. The ASTA study measures the adherence to standard treatment with methylphenidate using an electronic Medication Event Monitoring System (MEMS).

Fragile-X-Syndrome:

The Fragile-X-Syndrome is one of the most common causes for heritable mental retardation. The syndrome is based on a gene mutation at the x-chromosome with mental retardation ranging from mild to severe cognitive impairments. In addition to cognitive impairments, speech disorders and attention deficits are presented. A new drug is being tested in phase-III-trials for adolescent as well as adult patients with this disorder.

Healthy Subjects (Medicine and Dental Students):

In cooperation with the dean of the University Medicine Mainz we established a mindfulness based stress prevention program. "MeditMind" is based on both mindfulness awareness, hyperactivity and impulsivity with functional impairments in daily activities. Primary issues of interest include treatment procedures (pharmacological and supplement based) and measurements of adherence in pharmacological treatment. The FAD study seeks to analyse treatment outcomes with polysaturated fatty acids like fish oils whereas the Guanfacine study targets a drug, initially prescribed for the treatment of high blood pressure in adults, in the treatment of ADHD. The ASTA study measures the adherence to standard treatment with methylphenidate using an electronic Medication Event Monitoring System (MEMS).

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Department of Psychosomatic Medicine

The clinic provides inpatient treatment with 24 beds and day hospital treatment for 28 patients. Our multimodal treatment concept takes into account acute and chronic physical, mental and social causes of disease. On a psychodynamic background we integrate body oriented, creative, behavioral and systemic treatment approaches.

Specialized outpatient units offer assessment, consultation and treatment, esp. for the depersonalization-depersonalization syndrome, posttraumatic stress disorders, behavioral addictions (Grüsser-Sinopoli outpatient clinic) and sleep disorders. Our sleep laboratory offers polysomnographic assessment. Consultation-liaison services are provided to all patients of the UM Mainz to cope with stressful medical disorders or procedures (e.g. transplantation surgery).

Our postgraduate curriculum qualifies psychologists and physicians as psychodynamic psychotherapists or psychoanalysts, offering outpatient psychotherapy in its training institute.

The associated institute of medical psychology and sociology has focused on neuroscience research, and research on improving medical training (e.g. by patient actors).

Center for translational vascular biology
Psychosocial factors play a major role in the etiology and course of cardiovascular disease. As one of the core units of the Gutenberg Health Study, the department of psychosomatic medicine investigates the interaction of personality, mental disorders (depression, anxiety, depressive disorder), cognitive function, health behavior and cardiovascular disease. Specific treatment approaches have been developed and tested for patients with cardiovascular disease. In a multicenter randomized controlled trial (RCT) we have participated in evaluating a novel psychotherapeutic approach to improving illness coping, healthy lifestyle and emotional regulation in depressed coronary patients. In a randomized stepped care approach, the contribution of psychomotoric motivation training (vs. care as usual and sports medicine consultation) is tested promoting exercising and physical fitness after stent implantation in coronary heart disease. Studies are conducted in close collaboration with the center for Translational Vascular Biology, the center for thrombosis and hemostology, cardiology, medical statistics and laboratory medicine.

Translational neuroscience
In neuroimaging studies (fMRI, PET, EEG) we investigate biological mechanisms of mental disorders, e.g. emotion regulation in depersonalization, somatiform disorders (“Theory of Mind”), internet addiction (reward system) and effects of psychotherapy on emotion regulation (panic disorder, pathological gambling) in collaboration with the Center for Translational Neurosciences. We have established a shielded EEG laboratory in order to study attention and emotional processing in mental and psychosomatic disorders.

Psychoneurology
The department of psychosomatic medicine represents psychoneurology in the University Cancer Center (UCT). Recently, we have conducted studies funded by the German Cancer Aid alleviating depression in breast cancer patients by psychodynamic short-term psychotherapy, and assessing the quality of life of long-term survivors of malignant melanoma in a register-based study (cooperation with IMEL and the Cancer Registry).

Psychotherapy research
We have been conducting numerous RCTs to establish (and improve) the efficacy of psychodynamic short-term outpatient treatments of anxiety disorders (panic disorder, social phobia), and long-term outpatient treatments of depression. We have also participated in multicenter observational trials on the effectiveness of inpatient and day hospital treatments in depressed patients. A special expertise is related to quality assurance (competence and adherence ratings of video recordings of sessions, process research) and to manualized psychodynamic treatments (which are published in a new series). In the postgraduate psychotherapy training program, we aim at integrating novel psychotherapy and training research findings, and establish practice-research networks in order to further qualify therapists to perform clinically relevant process-outcome research. In the interdisciplinary DFG-funded Graduate College Life Sciences-Life Writing we study patients’ narratives undergoing psychotherapy.

Attachment research
Attachment is a basic dimension underlying normal and pathological development and the success of psychotherapy. In multidisciplinary studies we determine associations between childhood trauma, attachment patterns, emotion regulation, gene toxicity and mental representation and biological markers of oxytocine. Additional studies refer to post-partum mother–child attachment.

E Mental health and rehabilitation research
In an RCT we have tested the effect of a psychodynamic online intervention on vocational reintegration, and we are currently developing novel online approaches on preparing patients for psychotherapy and on supplementing self-guided online support to inpatient psychotherapy. A junior research group has been formed dedicated to the development of e-mental health collaborating closely with the Research Unit Media Convergence.

Sabine M. Grüsser-Sinopoli Outpatient Clinic for Behavioral Addiction
As the first specialized outpatient unit in Germany, the clinic has been active defining standards for research, diagnosis, care and prevention in the rapidly evolving field of behavioral addictions. The clinic offers the whole range of medical care for a broad range of behavioral addictions (online gaming, online sex and other internet addictions, pathological gambling): an anonymous and free hotline, assessment, consultation, innovative and manualized cognitive-behavioral individual and group treatments, day hospital and inpatient care (resp. referral to inpatient rehabilitation), outpatient rehabilitation and aftercare (pathological gambling). As there is a lack of sound research and consensus regarding the novel phenomena of online addictions, the clinic is also dedicated to German and international epidemiological, neurobiological studies, and it has initiated the first international RCT on treatment efficacy for computer gaming and online addictions. The third mission refers to establishing cooperation and evaluation of effective preventive measures protecting participants of all kinds of gambling.
The Department of Neurology consists of a total of 66 beds including a nationally certified Stroke Unit outfitted with state-of-the-art equipment, as well as additional beds for neurological patients requiring intermediate and intensive care. In addition to the inpatient facilities, the Department of Neurology also has nationally renowned specialized outpatient clinics with particular emphasis on the treatment of multiple sclerosis and other inflammatory diseases of the nervous system, pain, epilepsy, neuromuscular diseases and neuro-oncology. In the outpatient clinic for movement disorders in cooperation with the Department of Neurosurgery, consultation is provided on the operative treatment of Parkinson’s disease through deep-brain stimulation and other methods.

**MAIN FOCUS OF RESEARCH**

The primary focus of our research is in the field of neuroimmunology – classical inflammatory diseases as well as inflammatory and defense mechanisms in strokes and brain tumors. As part of this research, we are investigating the pathogenesis of inflammatory neurological diseases using cell-culture and animal-model experiments, patient examinations, imaging, and genetics. An example of this research is the use of two-photon laser scanning microscopy to directly investigate the behavior of immune cells in inflammatory lesions in the brains of living organisms. The fundamental knowledge gained in such experiments forms the basis for translational and clinical-experimental research, from which practical applications for patients can be derived. Research is conducted in close collaboration with other scientists in the Johanna Gutenberg University Mainz through our active participation in the Focus Program for Translational Neurosciences (FTN), Research Center for Immunotherapy (FZI) and German Resilience Center (DRZ), as well as with neuroscientists in the Rhine-Main region as part of the Rhine-Main Neuroscience Network (rM2).

Genetic funding for this research has so far been secured from the German Research Foundation (DFG) and Federal Ministry of Education and Research (BMBF). Together with the Universities of Munich and Mainz, we are part of a DFG-funded Collaborative Research Center “Initiating/effector versus regulatory mechanisms in Multiple Sclerosis – progress towards tackling the disease,” which aims to elucidate the foundations of multiple sclerosis to gain a better understanding of its pathophysiology with the goal of finding new targets for treatment of the disease. From a practical point of view, with the support of the BMBF, we have aligned ourselves with the largest specialized centers for Multiple Sclerosis in Germany as part of the patient-oriented “Competence Network for Multiple Sclerosis (KKNMS),” whose purpose is to improve treatment of MS patients as well as strengthen clinical research through multi-center cooperation.

The regimen and mechanisms of neuroprotective medications, and the roles of action of proteins and signaling pathways represent another important area of our research. We utilize models to study the cellular and molecular foundations of here-aldy and acquired neurodegenerative illnesses in order to gain a deeper understanding of new therapeutic approaches. For example, we are investigating the pathophysiology of hereditary polyneuropathy of nerve cells using stem cells from affected patients.

For both in- and outpatient, the Department of Neurology offers the following neurophysiological examination methods: Doppler ultrasonography; electrophysiology with nerve conduction tests and electromyography; somatosensory, visual and motoric evoked potentials; electroencephalography (EEG); electrocorticography; as well as autonomic functional and quantitative sensory tests. Video-EEG facilities are available to determine potential indications for the surgical treatment of epilepsy in patients with therapy-resistant epilepsy.

Each year, the Department of Neurology cares for approximately 3000 inpatients, as well as treating 6000 outpatients.

**Fig. 72:** Two-photon microscope image of mouse brain for stroke research

**Fig. 73:** Neuroimmunological research laboratory

**Fig. 74:** MRI analysis of brain affected by multiple sclerosis

**Important Publications**


Leuenberger T, Pateman M, Routier E et al. The Role of CD4+ T Cells and Their Local Interaction with CD8+ T Cells in Myelin Oligodendrocyte Glycoprotein (35-55)-Induced Experimental Autoimmune Encephalomyelitis. JOURNAL OF IMMUNOLOGY. 2013, 191 (49): 4960-4968.

Lill CM, Schijfels BM, Gisaret C et al. MANBA, CIXCR, SODA, RPS6KB1 and ZBTB8 are genetic risk loci for multiple sclerosis. BRAIN. 2013, 136: 1778-1782.


**Main Focus of Research**

The Department of Neurology offers the following neurophysiological examination methods: Doppler ultrasonography; electrophysiology with nerve conduction tests and electromyography; somatosensory, visual and motoric evoked potentials; electroencephalography (EEG); electrocorticography; as well as autonomic functional and quantitative sensory tests. Video-EEG facilities are available to determine potential indications for the surgical treatment of epilepsy in patients with therapy-resistant epilepsy.

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The Center for Childhood and Adolescent Medicine (ZKJM) at the University Medical Center Mainz serves as a hospital for supra-maximum medical care and is the only aca-
demic child health institution in the state of Rhineland-Palatinate. The children's hospi-
tal provides comprehensive pediatric care
for the population of Mainz and the surround-
ing regions. In addition, state-of-the-art medical treatment is available for all rele-
vant pediatric subspecialties, such as neo-
natal and pediatric intensive care, emer-
gency medicine, pediatric oncology, cardiology, endocrinology, gastroenterology,
fungal diseases, immunology, nephro-
logy, pulmonology, metabolic diseases and
neuroepidemiology. On average 6,000 inpa-
tients and approximately 14,000 outpatients
are treated each year in the ZKJM. Beyond
that, numerous research projects especially
in the field of pediatric metabolic diseases,
immunology and infectious diseases, mole-
cular genetics and endocrinology funded by
national and international organizations
are conducted. The ZKJM is highly reputed for
its expertise in clinical trials comprising
investigator and externally sponsore-
d clinical trials following GCP and GLP
standards.

STRUCTURE, FUNCTION AND ORGANISATION OF THE CENTER

Pediatric Oncology and Hematology

A major research focus is the analysis of
epidemiology, pathobiology and genomic/
epigenetic predisposition of late effects
in childhood long-term survivors as part of
the newly established “Mainz childhood
cancer survivor program”. Evidence is
accumulating that a broad spectrum of
late-effects, especially early-onset cardio-
vascular disease - together with a relapse
of the malignancy or a de novo second
malignant neoplasm – cause significant
morbidity and mortality in long-term survi-
vors. Current projects investigate clinical,
epidemiological and genetic aspects of
late effects related to pediatric cancer ther-
apy.

Neonatology

The Department of Neonatology performs
everal clinical studies – mostly in context
of interdisciplinary collaborations. A retro-
spective analysis evaluates the outcome of
preterm infants <1500 g birth weight rela-
ted to the mode of delivery, either by cesa-
rean section or vaginal delivery. A prospec-
tive observational study compares the
duration of weaning preterm infants from
CPAP either following a standardized pro-
tocol or by an individualized approach. A
prospective study investigates the rele-
sance of viral agents for nosocomial infec-
tions in newborns who receive antibiotic
treatment due to suspected bacterial
nosocomial infection.

Neurology

The research focuses on the investigation of
the pathogenesis of lysosomal storage
diseases and the development of genetic
engineering methods for therapy by
enzyme replacement and/or substrate
reduction. Clinical research projects are
concerned with bioengineered therapies
for patients with mucopolysaccharidosis,
Fabry’s, Gaucher’s, Pompe’s and Niem-
mann-Pick disease.

Molecular Pediatrics

The research group is investigating the
physiological role of ion channels of the
TRPM superfamily and the effect of dys-
regulation or mutation of the corresponding
genes. A key research focus here is the
TRPM5 channel - first discovered by this
group- and its relevance in hormone
release (e.g. insulin) as well as the signifi-
cance in disorders with corresponding
endothrinological defects. An further pro-
ject investigates the role of TRPM7 in the
tumor genesis.

Pediatric Infectious Disease

The research focuses on epidemiologic
studies of respiratory pathogens, the gut
microbiome and experimental vaccinology.
The epidemiological centerpiece is a multi-
plex-PCR-system suitable for the survei-
nance of 19 different respiratory patho-
gens. Data on the epidemiology of infections with these pathogens provide a
comprehensive, long term overview of the
prevailing pathogens. In addition an array
based detection platform is under devel-
omeent. In order to improve the under-
standing of the pathogenesis of chronic
inflammatory bowel diseases comparative
microbiome studies in affected children
and their healthy siblings are performed.
Finally, supported by the German Research
Foundation (DFG), we investigate the pro-
erties of polymeric nanocarriers as a
novel vaccine platform, allowing the simul-
aneous delivery of antigens, adjuvant and
targeting receptors.

Pediatric Immunology

The research projects focus on the char-
erization of the immune system of
newborn infants: autocrine effects of den-
drritic cell-derived IL-27 and its compensa-
tory effects on the limited availability of
IL-12 in neonates; cross-sectional study
on IL-27 expression during childhood; rele-
vance of IL-27 in neonatal sepsis; regula-
tion of IL-21 production in the pediatric
population and its therapeutic options;
importance of cytokine expression for the
susceptibility for infectious diseases;
maturatin of neonatal Dendritic Cells and
vaccine optimization for early immuniza-
tion of infants; effects of trc1/2 gene
defects on inflammatory processes in
monocytes from pediatric patients with
tuberous sclerosis; T-cell-mediated regula-
tion of the immune response after vacci-
nation.

Pediatric Rheumatology

The group studies mechanisms of the
adaptive and innate immune system in the
pathogenesis of juvenile idiopathic arthri-
tis (JIA) and of auto-inflammory bone
disease (CRMO) in children and ado-
lescents. The projects are concerned with
the phenotype expression of T and B cell
differentiation markers and the analysis of
pro- and anti-inflammatory cytokine
expression on mRNA and protein levels.
Moreover, in the vitro regulation and the
activation patterns of dendritic cells are
under investigation.

Fig. 7B: Center for Childhood and Adolescent Medicine (ZKJM)

IMPORTANT PROJECTS | MAX. 5

Cardiac and vascular late sequelae in long-term survivors of childhood cancer (CVSS-study)
Project Manager: Prof. J Faber, PD Dr. C. Spa, Prof. F. Will
Project Duration: 2013 - 2017

Diseases caused by imprinting defects: clinical spectrum and pathogenetic mechanisms. Sub-
project 5: Interaction of imprint chromosomal domains (BMFB)
Project Manager: Prof. D Prawitt
Project Duration: 2012 - 2015

Gastroenteritis due to rotavirus in childhood - Burden of disease
Project Manager: Dr. F Kowalczy
Funding: Sanofi Pasteur MSD
Sum: € 150,000
Project Duration: 2011 - 2013

MORS (Morquio Studies)
Project Manager: Dr. E Mengel
Funding: Biominar
Project Duration: 2010 - 2015

Non-immunological hydrops fetalis – retrospective analysis and prospecti-
ve register
Project Manager: PH Dr. C Wibhaus-TRAIN-
ler, Prof. E Mildenberger
Cooperation: Prof. M Beck (villa metaboli-
cal), Dr. E Mengel (Villa metabolica), Dr. S Macchilla (fumonoligiy) et al.
Funding: Rheinland-Palatinate, University
Part II
Sum: € 31,800
Project Duration: 2012 - 2017
Surgery Departments

- Center of Orthopedics and Trauma Surgery (ZOU)
- Department of Ophthalmology
- Department of Otorhinolaryngology, Head- and Neck surgery
- Department of General-, Abdominal and Transplant Surgery
- Department of Obstetrics and Gynecology
- Department of Cardiothoracic and Vascular Surgery
- Department of Pediatric Surgery
- Department of Neurosurgery
- Department of Urology
- Department of Anesthesiology
The Center of Orthopedics and Traumatology, as one of the biggest facilities of the University Medical Center Mainz including 120 inpatient beds. It provides services for a wide range of musculoskeletal system injuries and diseases. It performs more than 4,500 surgical interventions per year. With our motto of ‘Our Expertise for Your Health’ we are always eager to help patients in the best possible way through application of our scientific knowledge and longstanding experience in medical healthcare within the state-of-the-art facilities.

The Department for Orthopedics and Traumatology was recently formed out of the merger of the Department of Traumatology and the Trapeak Clinic of the University Medical Center. The decision to merge the departments was made to pool expertise and resources as well as to eliminate redundancies, which were visible in many fields like spine surgery and arthroplasty. With this broader view of musculoskeletal disorders’ different pathologies, we develop common sub-specialties and improve our quality of care. In the new Department, specialists with broad expertise in both orthopedics and orthopedic trauma surgery represent different subfields, such as hand surgery and reconstructive trauma surgery. This strengthens the visibility and transparency of their disciplines for colleagues, students and patients.

Polytrauma, Pelvic and Acetabular surgery

The team of polytrauma, pelvic and acetabular surgery has a broad expertise and a long-standing experience in this field, which is reflected in numerous national and international publications as well as in participating in various panels of experts. The proper after-treatment of patients is organized in a specialized outpatient consultation.

Shoulder and Knee Surgery

The treatment spectrum covers the shoulder surgery from almost complete and includes the modern arthroscopic methods for reconstruction as well as shoulder arthroplasty using modern implants. Besides the well-established standard care, revision surgery of the knee joint has been established as an additional focus in our department. Due to an increasing number of nationwide primary arthroplasties of the knee joint as well as to increasing life expectancy the need for revision surgery increased dramatically in the last years. Our broad experience in this field and the use of different systems allows us to respond in every case individually to a specific situation.

Extremity traumatic and reconstructive joint surgery

For treatment of severe limb and joint injuries we provide our broad expertise in the whole surgical spectrum including reconstructive microsurgery and plastic surgery. In cases of severely damaged, non-reconstructable joint injuries modern endoprosthetic techniques are available for joint replacement. Our spectrum also includes the treatment of fracture non-unions as well as posttraumatic joint deformations.

Hand and Elbow Surgery

The surgical spectrum in this field includes the entire open, arthroscopic, endoprosthetic and microsurgical hand and elbow surgery. A thorough knowledge of soft tissue coverage ensures a prudent and thorough surgical removal of bone, soft tissue, and skin tumors of the upper extremity. Degenerative diseases with high numbers of surgical interventions including total elbow replacement interventions are also in the main field of our hand- and elbow surgery team.

The department for orthopedics and traumatology is focused on different interdisciplinary network projects in the field of the regenerative medicine and development of novel implants for fracture care. Many biomechanical studies are being performed in a modern equipped laboratory for biomechanics. The focus of our developments lies on problematic fracture types of the lower and upper extremities and of the spine. Thereby, various prototypes have been developed for implants that are currently used worldwide for fracture care, such as the proximal humerus nail (PHN, Synthes Company) and the expert tibia nail (ETN, Synthes Company). Furthermore, we perform many comparative studies with already established implants to identify best-suited implants for specific indications. In a collaborative work with the University for Applied Sciences Wiesbaden (Prof. Hel) we developed a spine simulator for the development and testing of spine implants. Many companies such as Synthes Bettlach GmbH, Medartis GmbH are our industrial partners in this field.

Fracture healing and bone defect reconstruction has been one of the major topics and interests of our research for many years. Our department is a member of a research platform in the Mainz University Medical Center named BioMaTIC – Biomaterials, Tissues and Cells in Science. In a modern cell- and molecular biology laboratory we perform in-vitro and in-vivo studies about the interaction between cells and materials. We provide a broad expertise in the assessment of interaction between bone cells and materials. We provide a broad expertise in the assessment of interaction between bone cells and materials.
Department of Ophthalmology

The Department of Ophthalmology of the University Medical Center Mainz is one of the largest facilities of its kind in Germany – in terms of health care as well as research and teaching. In 2013 approximately 5,700 patients received inpatient treatment in the Department of Ophthalmology, while ambulant surgery was carried out 2,700 times and approximately 55,000 patients were treated ambulant. The department offers special consultations for various diseases including age-related macular degeneration (AMD), Graft versus Host Disease (GVHD), Glaucoma and Keratoconus as well as corneal, orbital, macular diseases and tumours. In order to provide specific treatment for the different clinical pictures, further consultations offered include the topics contact lenses, eye lid, retinal lasers and refractive surgery.

Adaptation of visual aids (Low Vision Aids), a comprehensive diagnostic department for the diagnosis and documentation of the course of diseases, as well as a histopathological department, complete the therapeutic range.

In 2013 the Cornea Bank of Rhineland-Palatinate, operated by the Department of Ophthalmology, was again among the three largest facilities of its kind in Germany. Existing collaborations include national and international partners such as the German Foundation for Organ- and Tissue Transplantation (DGfG). In 2013 it was possible to obtain a total of 673 corneas and 359 patients received a cornea transplant, 127 of which were treated at the Department of Ophthalmology in Mainz.

**MAIN FOCUS OF RESEARCH**

Based on the above health care the research can be divided into the following 4 areas:

Epidemiology and health care research Numerous research projects are conducted at the Department of Ophthalmology as part of the large-scale European Health Study (GIS). The working group „Ophthalmological Epidemiology“ continued its work in 2013 with a focus on prevalence survey of important eye diseases and epidemiological genetics in the context of the interdisciplinary, population-based GIS. Part of this work is the investigation of ocular phenotypes by genome-wide association studies (GWAS) for the determination of their genetic basis. These evaluations are mainly performed in international consortia (Consor- tium for Refractive Error and Myopia (CREAM), International Glaucoma Genetics Consortium (IGGC) or European Eye Epidemiology (E3) Consortium). Among others, investigations in this research area include the frequency of glaucoma and the occurrence of congenital and juvenile glaucoma, the distribution of the intracocular pressure, the morphology of the optic nerve and the corneal thickness, as well as their association with ocular and systemic parameters. Producing nine publications in 2013, this year has been the most successful year for the working group so far. Among others, the working group could successfully show correlations between increased intracocular pressure and cardiovascular features.

Clinical Study Center The Clinical Study Center of the Department of Ophthalmology is certified within the framework of the European Vision Institute Clinical Trials. Sites of Excellence (EVI. CTS). During the year 2013 numerous clinical studies, including external studies, internal studies (studies for medical devices, pharmaceutical studies) and scientifically initiated clinical studies were performed with great efficiency. The Study Center is also involved in the FP7-Project "STROMG" sponsored by the European Commission which investigates the prevention of neovascular glaucoma following an ischemic central vein occlusion. This multi-centred study with eight partners and intends to involve 333 patients in 35 study centres throughout Europe. The study receives 5.7 Mio Euro funding from the EU.

Experimental and translational Ophthalmology The division of “Experimental and Translational Ophthalmology” focuses on clinic-related basic research while using state-of-the-art analysis methods from proteomics and immunology to investigate the pathomecha- nisms of various ocular diseases. Particularly noteworthy is the proof of retinal anti- body deposits in patients with glaucoma which could be demonstrated for the first time in the year 2013. These findings are consistent with our previous studies and can thus emphasize the immunological aspects of glaucoma. Another part of the institutes work is the determination of new biomarkers for early diagnosis and thera- peutic approaches of different diseases (AMD, glaucoma, dry eye disease). The newly identified biomarkers are then further investigated in cell culture experiments and animal studies. For this purpose the project “Autoantibodies in glaucoma: importance for early diagnosis and treatment” received funding from the “Stiftung Rheinland-Pfalz für Innovation” from the German State Rheinland-Palatinate in 2013 and, additionally, different projects that focus on the research of the role of antibodies in AMD were industrially supported. Numerous projects in basic research are conducted as part of the internal university research funding programs (MAIFOR, Internal University Research Funding (Stage 1) or the Science-Transfer-Program of the Uni- versity Medical Center Mainz). These projects include the determination of new methods for the diagnosis of glaucoma in patients with Mukopolysaccharidosis or the study of correlations between oxidative stress and glaucoma. Further projects investigate the regulation of ocular pressure through mucinetic acetylated cholinesterase subtypes (laboratory for ophthalmobio- mophysics) and the influence of prostaglandin and betulinic acid on the development of a reti- nal ischemia-reperfusion injury.

Clinical research and development The close cooperation at the University Medical Center Mainz can be seen in many interdisciplinary collaborations. Thus, the Department of Ophthalmology shares the project „New risk factors for retinal vein occlusions” with the Center for Thrombosis and Hemostasis (CTH) and performs proteo- mic investigations concerning endocrine orbitopathy in patients with M. Basedow in cooperation with the division of “Endocrinology and Metabolic diseases” from the Department of Medicine I.

As a newly initiated developmental project in 2013 the „Development and clinical testing of a new subjective glaucoma examination method “PAKO“ (“pattern noise”) with parti- cular suitability for the cost-effective use in African developing countries” was started.
The Department of Otorhinolaryngology, Head and Neck Surgery encompasses four wards with in total 80 beds including two beds in the sleep laboratory, one children’s medical unit and one intermediate care ward. About 4,000 patients are treated each year. In the seven available operating rooms over 6,000 surgeries are performed per year. Surgically, the entire field of ear, nose, and throat medicine is covered. Core areas of expertise are the treatment of acoustic neuromas and skull base surgery. In addition, all middle ear surgeries are performed for hearing improvement and treatment of chronic inflammation. Another focus of the clinic are cochlear implant (CI) operations in children and adults. Furthermore, microsurgical operations of the nose and paranasal sinuses are implemented and applied both minimally invasive laser surgical procedures and open surgical procedures for treatment of tumors in the head and neck. The conservative therapies extends from the implementation of tumor chemotherapy to diagnosis and treatment of allergies, and beyond to complex oto-neurological diagnosis of vertigo. In the division of communication disorders about 3600 patients with speech and language disorders, voice and swallowing disorders as well as children and adolescents with hearing disorders are examined per year, mainly on an outpatient basis. Children with severe developmental language disorders and hearing disorders are treated on a ward.

In order to guarantee an optimal and innovative patient care now and in the future, ENT typical disease patterns are explored in detail in the faculty. The key research areas can be considered as continuous translational developmental processes beginning from open operations to molecular-based treatment-, and prevention methods.

Otology and communication disorders

With the aim to improve hearing impairments we analyze the molecular causes and optimize treatment strategies by introduction of novel therapies in daily clinical practice. In the future, increasingly the body’s own molecular protection mechanisms will be recruited for prevention and treatment of hearing loss. Data suggest specific proteins such as the cellular protective protein survivin, which ensures protective protein survivin, which ensures that children with hearing loss demonstrate very different speech and language development, which does not depend solely on the degree of hearing loss, but also on various other factors. We found an increasing incidence of functional hearing impairments, i.e., somatosensory disorders in children, resulting in impaired hearing despite normal physical conditions, because they cannot withstand stress of everyday life.

RhinoLOGY

Allergies are increasingly occurring and thus, have a significant socio-economic impact. Our research centers on the identification of major factors and disease mechanisms involved in chronic inflammation of the nose. Polyps are common but despite normal physical conditions, because they cannot withstand stress of everyday life.

Oncology

The mission of translational oncology is to exploit our comprehensive knowledge from basic research for the prevention and therapy of patients with head and neck cancer. Cellular mechanisms regulating survival and damage-repair are not only key to regenerative medicine but also for tumor development and progression. As such, these molecular regulations significantly impact also response to therapy, quality of life and survival of cancer patients. Hence, we specialize on the identification of mechanisms contributing to irradiation- and/or chemo-resistance of tumors as well as the on the development of interference strategies. Research is performed in close collaboration with the UMM’s main research areas “Tumourbio- medicine”, “Immunology” and the initiative “Chemical BioMedicine”. Besides key publications in leading cancer and nano-biomedical journals, the success of our work is underlined by a recent patent application of novel anti-fungal drugs. To evaluate and further promote the clinical transfer of our knowledge, we are interacting with the CHiR-Net and IGKS in order to optimally design and execute preclinical trials.
The Department of General-, Abdominal and Transplant Surgery consists of two departments, fused in October 2012. In the year 2013 3535 patients were treated (74 beds and 4 intermediate care beds). In addition, about 5952 cases were treated in our outpatient clinic. Altogether about 3334 operations and 49 liver transplantsations were conducted.

In particular close interdisciplinary with the Department of Medicine (I. Med. Klinik, Department of Gastroenterology and Hepatology), the Department of Diagnostic and Interventional Radiology, the Department of Radiation Oncology and Radiation Therapy provides high quality treatment before, during and after surgery respectively transplantations.

Intercalary tumorbords guarantee optimal treatment for each tumor patient based on current guidelines. Also, eligibility for modern treatment concepts or inclusion in clinical trials is evaluated and recommended in these boards.

Our department has been certified as competence centre for Hepatobiliary, for Endocrine and Upper Gastrointestinal surgery underling the high standards of our department.

The Department of General-, Abdominal- and Transplantation-Surgery includes the following categories of special expertise in visceral surgery:

- Upper gastrointestinal tract (esophagus, stomach, duodenum)
- Emphasis lies on oncologic surgery and minimal-invasive techniques in the gastrointestinal tract and esophagus, especially on gastrointestinal reflux disease and achalasia.
- Sarcoma, peritoneal carcinomatosis and HIPEC
- Multidisciplinary treatments of retro- and intraabdominal sarcoma, frequently as interdisciplinary surgical approaches with Urology and Gynecology, or surgical therapuy of peritoneal carcinomatosis (peritoneectomy) in combination with heated intra-peritoneal chemo/perfusion (HIPEC) are standard procedures in our department.

Endocrinology
In addition to established minimal-invasive techniques for thyroid- or parathyroidectomy, also adrenolecetomy and segmental resection of pancreas are routinely performed by laparoscopy.

Lower gastrointestinal tract (small intestine, colon, rectum, anus)
Laparoscopic surgery has become the standard approach for most benign and malignant diseases and are conducted on a high level. A main focus of research lies in the continuous intraoperative monitoring of pelvic autonomic nerves during total mesorectal excision (TME) to prevent urogenital and anorectal dysfunction in rectal cancer patients.

Liver, biliary and pancreatic diseases
Hepatobiliary and pancreatic surgery is a major focus of our department, in particular bile duct cancer as well as primary and secondary liver tumors. More than 300 liver resections are performed per year. All surgical techniques are offered including operations on in situ cooled liver, laparoscopic hepatic resection and in situ split procedures. The use of computer-assisted risk analysis are frequently used for planning of major hepatectomy and especially for intraoperative navigation of liver resections.

Liver transplantation
In 2013, forty-nine liver transplantations were performed for the following indications: acute liver failure, hepatocellular cancer, cholestatic liver diseases, cirrhosis of different origins, metabolic liver diseases. A specialized outpatient clinic provides care of patients before and after transplantation.

Tumor follow-up care
Postoperative treatment and follow-up care is offered in close collaboration with other departments and clinics. Data are collected for optimizing therapy and research.

In addition to the development, evaluation and implementation of innovative surgical procedures our research focus is mainly on oncology. The characterization of the biology of primary tumors and metastases is analyzed by molecular biology and many clinical analyses in order to identify prognostic markers and targets for future treatments.

The section of Endocrine Surgery focuses on the treatment of benign and especially malignant thyroid diseases as well as diseases of the parathyroids, adrenals, endocrine pancreas, neuroendocrine tumors of the gastrointestinal tract and paragangliomas. Beside established laparoscopic methods all kinds of minimal-invasive techniques like thyroid- or parathyroidectomy, adrenalectomy, partly resections of pancreas are performed. Intraoperative neuromonitoring is routinely used and further evaluated in cooperation with interna study groups. The generic characterization of thyroid carcinomas as well as of other endocrine tumors is one of the main research areas. In the sense of translational medicine the results are used to identify thyroid carcinomas preoperatively and to optimize postoperative treat-ment strategies.

Liver transplantation research focuses on the treatment after liver transplantation (e.g. immunosuppression), long-term results of patients with hepatocellular cancer, prevention of bile duct damage and arterio-thrombosis.

Continuous intraoperative monitoring of pelvic autonomic nerves during total mesorectal excision (TME) to prevent urogenital and anorectal dysfunction in rectal cancer patients is one of the key projects; this import topic will be further developed and tested in future studies.

The evaluation of two-dimensional intraoperative neuromonitoring for predicting urinary and anorectal function after rectal cancer surgery was a special sub-subject done by D. W. Kaufl published in “International Journal of Colorectal Disease”.

In addition, the characterization of genes involved in the regulation of the organic cation transporter 1 (SLC22A1) is associated with tumor progression and reduced patient survival in human cholangiocellular carcinoma.

Project manager: Dr. A Lautem, PD Dr. T Schacht
Project Duration: 2012 - 2013

Genetic and immunohistochimetic characterization of poorly differentiated thyroid carcinoma (PDTC)
Project manager: Prof. T Nuchter, Dr. A Schulz, T Gerber
Project Duration: 2013 - 2015

Identification of risk genes for achalasia
Project Manager: Prof. I Goebel
Cooperation: PD Dr. J Schumacher (Institut für Humangenetik, Universitäts- klinik Bonn), PD Dr. M Kopp (Institut für Medizinische Biometrie, Universitätskli- nik Bonn)
Funding: German Research Foundation
Sum: € 280,000
Project Duration: 2012 - 2013
A major focus of research is the examination of prognostic and predictive factors in breast cancer and ovarian cancer. Based on these results, a gene-expression signature for risk assessment for patients with estrogen receptor (ER)-positive and human epidermal growth factor receptor 2 (HER2) negative is already commercialized (endoPredict®, Sividon GmbH, Köln, Germany). Beyond that, the prognostic and predictive influence of tumor-infiltrating B-cells and especially plasma cells in breast cancer was first described by PD Dr. M. Schmidt. These novel findings will be extended both to other entities like ovarian and endometrial cancer as well as to breast cancer patients treated with adjuvant therapy. In addition to gene-expression analyses and immunohistochemistry we performed next generation sequencing on well-characterized breast cancer specimens in collaboration with the Institute of Translational Oncology (TrON), University medical center Mainz. Building on those results, we are collaborating with BioNTech AG, Mainz, Germany, to take a novel individualized vaccination strategy aiming at tumor-associated antigens in triple-negative breast cancer (TNBC) to the clinic. Another advancement of our research dealing with the prognostic and predictive capabilities of tumor-infiltrating plasma cells is collaboration with Bayer Technology Services GmbH, Leverkusen, Germany. Here, we aim to isolate tumor-infiltrating lymphocytes, especially plasma cells, and amplify and characterize their immunoglobulin repertoire with single-cell RT-PCR to develop an antibody library. In a next step, we are conducting a study to characterize antibodies in the plasma of breast cancer patients and examine correlations of the antibody profile and pathological characteristics of the breast cancer as well as the outcome of the patients. In addition to the participation in numerous multicenter studies in gynecological malignancies, we conducted the neoadjuvant EXPRESSION study in breast cancer to develop a predictive gene-expression signature and we are currently conducting a multicentric psychosocial group intervention study to support the patient’s competence (Dipl.-Psych. G. Schöner). In gynecological oncology, a field of special research interest of Prof. R. Seufert is the Times Laps-system which allows the accurate determination of parameters of the endometric division and growth behavior which will provide new insights into the biological behavior of fertilized eggs and embryos by non-invasive techniques. They are characterized by image analysis techniques of texture, growth curves and kinetic data and are used to estimate prognosis. The aim is to predict implantation and thus the possibility to achieve pregnancy by a single transfer, which lead to a decrease in multiple births. A corresponding analysis program is developed. This data will be optimized with further biochemical and clinical parameters. Another project is the characterization of the secretion and activation mechanisms of human granulosa cells gained during follicular puncture. We are measuring receptors for growth factors, steroid and proteohormons such as Inhibin B, activin A and follistatin as a function of stimulatory peptide and patient population. Their influence on activation of different second messenger groups will be analyzed. In addition, a focus of research of Prof. R. Seufert and PD Dr. C. Skala is the level of anti-Müllerian hormone (AMH) which has a regulative function in the activation of folliculogenesis and is considered as a marker for the ovarian reserve. Until now, a relationship between AMH and oocyte retrieval number, antral follicle count, pregnancy rates and birth rates is known. To further assess the role of AMH, 1295 patients who underwent an IVF/ICSI treatment with FSH stimulation and had an evaluation of the serum AMH level before treatment were examined in a large-scale retrospective study. In urogynecology, PD-Dr. C. Skala and Dr. S. Albring compare the classical tension-free vaginal tape with novel mini sling in a prospective clinical study. In conclusion, the research in the Department of Obstetrics and Gynecology covers all aspects of this field.
The Department of Cardiothoracic and Vascular Surgery has two cardiac surgical wards with monitoring beds, an intensive care unit and a thoracic surgical ward. In the spirit of multidisciplinarity this ward is also occupied with vascular surgical patients. In addition, Mainz offers a certified vascular surgical center with main treatments in aortic diseases, the Peripheral Arteries, Occlusive Disease (PAD) and diseases of the carotid artery. Likewise Mainz has an endocrinoologically-vascular surgical ward where specifically patients with diabetic vasculopathy in cooperation with the internist colleagues can be treated patient-specific. The surgical procedures are performed in five operating rooms. In addition, cardiac surgery is performed at St. Joseph’s Hospital in Wiesbaden. About 1500 cardiac surgeries, 1200 vascular surgeries and 500 thoracic surgical procedures are performed per year.

**The focus of care of the department:**

**Cardiac surgery:**

The treatment of coronary heart disease and diseases of the aortic valve are the most common procedures. In addition, the treatment of diseases of the mitral valve, also as minimally invasive approach, as well as the treatment of thoracic aortic diseases (dissection, aneurysm) and acute care of pulmonary embolism are a focus in the treatment of cardiac surgery patients.

**Vascular surgery:**

Mainz offers a universal surgical therapy spectrum starting at the treatment of heart failure in the sense of rhythm surgery (pacemaker, defibrillator) from bypass or heart valve therapy to heart transplantation. In addition, our department together with our colleagues in cardiology offer a common hybrid surgery also minimalized methods for heart valve replacement, e.g. transapical or transfemoral valve implantation (TAVI). The thoracic surgery department offers the treatment of different pulmonary diseases starting from pulmonary wedge resections to lobectomies and minimally invasive procedures such as VATS (video assisted thoracoscopic) as well as a ultima ratio therapy the uni-or bilateral lung transplantation. Through the thoracic oncology cooperation in our hospital and the cooperation with the Catholic Hospital Mainz we are able to offer individual and specialized therapies for each patient.

The Department of Vascular Surgery also covers the full range: In addition to the treatment of peripheral arterial occlusive disease and carotid artery surgery, and venous and dialysis access surgery, our team is particularly specialized in surgically open procedures as well as endovascular replacement of the abdominal aorta and the thoracic aorta.

**The surgical procedures are performed in five operating rooms.**

**The focus on research:**

The research focuses on “Minimally Invasive Surgery” and “Vascular Therapy- and Research”. Within the activities of the Cardi thoracic and Vascular research we distinguish “function, tissue and material”. For Germany innovative ways are scientifically processed like the aortic register; Mainz is one of the reference centers. Under the subpriority “function” especially the process of intra- and intercellular signal- ling is systematically explored. Prototypically the Department of Cardiothoracic and Vascular Surgery has a special position, because of methods for the measurement of intracellular calcium, pH and sodium on the vital human heart muscle are offered under various model conditions. In a model of “skinned fiber” of the heart muscle different projects are running. Patients with mucopolysaccaridosis are investigated regarding to Ca-sensitivity and force capacity. Another research focus of this working group is the diastolic dysfunction and cardiac myxoid mitral valve degeneration. Furthermore it comes to strategies for organ preservation and ischemia and reperfusion. Fundamental work in the field “function” (sheer stress of extracellular matrix and morphology of extracellular matrix) are the main impulse for the common SFB initiative with neurosurgery “tissue-effector-interaction.” In the field “tissue” developments under the terms “tissue engineering” and „simulation“ are well advanced. A highly respected group with prices from the field vascular surgery developed pioneering prototypical models for the development of arteriosklerosis and biological vascular grafts. This should be an essential step on the pathway to biological implants. Similar pathways are done in cardiac surgery in the context of optimization of biological prosthesis. An important and young research area is the area of obesity research. It is of particular interest because it offers from the view of cardiac and vascular surgery the same clinical and scientific perspectives. Under the aspect “material” research on surface properties as well as innovative forms of extracorporeal circulation is performed. The night lecture series continue to enjoy great popularity, so that research focus „media convergence“ has developed together with the Mainz Institute for Book Sciences. The night lecture is considered the largest and most sustainable prevention project in the region.

**Main focus of research:**

The research focuses on “Minimally Invasive Surgery” and “Vascular Therapy- and Research”. Within the activities of the Cardiothoracic and Vascular research we distinguish “function, tissue and material”. For Germany innovative ways are scientifically processed like the aortic register; Mainz is one of the reference centers. Under the subpriority “function” especially the process of intra- and intercellular signal-ling is systematically explored. Prototypically the Department of Cardiothoracic and Vascular Surgery has a special position, because of methods for the measurement of intracellular calcium, pH and sodium on the vital human heart muscle are offered under various model conditions. In a model of “skinned fiber” of the heart muscle different projects are running. Patients with mucopolysaccaridosis are investigated regarding to Ca-sensitivity and force capacity. Another research focus of this working group is the diastolic dysfunction and cardiac myxoid mitral valve degeneration. Furthermore it comes to strategies for organ preservation and ischemia and reperfusion. Fundamental work in the field “function” (sheer stress of extracellular matrix and morphology of extracellular matrix) are the main impulse for the common SFB initiative with neurosurgery “tissue-effector-interaction.” In the field “tissue” developments under the terms “tissue engineering” and „simulation“ are well advanced. A highly respected group with prices from the field vascular surgery developed pioneering prototypical models for the development of arteriosklerosis and biological vascular grafts. This should be an essential step on the pathway to biological implants. Similar pathways are done in cardiac surgery in the context of optimization of biological prosthesis. An important and young research area is the area of obesity research. It is of particular interest because it offers from the view of cardiac and vascular surgery the same clinical and scientific perspectives. Under the aspect “material” research on surface properties as well as innovative forms of extracorporeal circulation is performed. The night lecture series continue to enjoy great popularity, so that research focus „media convergence“ has developed together with the Mainz Institute for Book Sciences. The night lecture is considered the largest and most sustainable prevention project in the region.
Department of Pediatric Surgery

Acting Director:
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The Department of Pediatric Surgery performs a wide range of services from routine hernia reduction to complex operations such as reconstruction for newborn anomalies and surgical removal of tumors. It is the only university institution in Rhineland-Palatinate which covers the entire spectrum of pediatric surgery. Specific strengths of the division include: minimally invasive surgery, comprehensive neonatal surgery, repair of chest wall deformities, treatment of hemangiomas and vascular malformations, management of complex trauma patients and burn injuries.

The minimally invasive techniques are commonly used for children at any age. The majority of operations are performed in the micro-laparoscopic technique (using 2mm instruments). A variety of even neonatal operations can already be carried out almost scar free. The Department of Pediatric Surgery provides world pioneering work in this area and is one of the leading European Pediatric Surgery clinics in this specialized field. In 2013 a new pediatric surgery operating room was built at the highest international standard. All minimally invasive surgeries can be performed in HD technique. The KARL STORZ OR1™ enables a centralized control of the entire operating room to manage endoscopic and peripheral devices and to view, display, document and communicate information from video and other data sources in and out of the operating room.

In the field of thoracic surgery, the focus is in minimally invasive as well as in the open correction of pectus excavatum and pectus carinatum using innovative materials (modified Nuss procedure, STRATOS). The treatment of severely burned children takes place in interdisciplinary collaboration with the pediatric intensive care unit (burn center with 2 pediatric intensive care beds). In cooperation with the Center for Orthopedics and Trauma Surgery, the Department of Pediatric Surgery is an important part of the Child Trauma Center with attached BG clinic. Furthermore, there is a close cooperation with the Pediatric Neurosurgery, with the local Perinatal Center (Level 1) and the local Department of Pediatric Oncology.

The key research project of the Department of Pediatric Surgery is the invention and development of new micro-laparoscopic techniques and devices with projects for instance to measure the optical parameters of the special 2.4 mm cameras. In 2013 we did develop a patentable anti-banding device for these optical systems. Furthermore, we did carry out various analysis with the LigaSure system for instance in appendectomy. New techniques have been described in a minimally invasive pediatric surgery surgical textbook. In the field of chest wall deformities and burn surgery we did closely work together with the BiomaTiCS group and other research groups within the university hospital.
Department of Neurosurgery

In 2013, 2200 in-patients were surgically treated at the Department of Neurosurgery. In addition, over 6000 out-patient visits were managed. We employ the most advanced surgical tools, from intra-operative, frameless image-guidance to minimally invasive skull base equipment. We partner with industry leaders to ensure that we have access to and even influence the next generation of surgical technology. Specializing in a range of neurological disorders, the Department of Neurosurgery focuses on patients with degenerative, traumatic or inflammatory diseases of the whole spine. We are providing a broad spectrum of minimally invasive techniques and modern instrumentation for spinal canal stenoses, disc herniations, spondyloolisthesis, vertebral fractures or spondylodiscitis. Further, our department is specialised in awake craniotomies for primary and metastatic brain tumors, cerebrovascular diseases (e.g. aneurysms, AVMs), functional and stereotactic surgery for e.g. Parkinson’s disease, movement disorders or epilepsy, and skull base surgery. Pituitary surgery for adenoma are routinely performed using 3D-guided endoscopy. Intracranial vascular diseases are evaluated by microvascular neurosurgeons and endovascular neuroradiologists in multidisciplinary conferences providing the patient both with option and the combined expertise of different therapeutic approaches.

One of the outstanding features of our Department is the possibility to perform minimally invasive robot-assisted surgery for brain and spine. Our multi-specialty Neurooncological Center is a highly developed facility were glioma as well as patients with brain metastases receive diagnostics, individualized tumor treatment including chemotherapy and psychooncological help.

In addition, we strive for the highest quality of neurosurgical care by providing neurosurgical knowledge and practice through research and innovation.

Scientifically the Department of Neurosurgery focuses on neurooncological research, complex spine surgery as well as the development of innovative 3D planning, simulation techniques, intraoperative navigation and operation techniques. New patients are regularly applied for. In our translational neurooncological laboratory emphasis is put on the research of malignant glioma and brain metastases. Our particular interest aims at characterizing tumor stem cells.

Fig. 90: Intraoperative 3D navigation for transphenoidal approach to the sellar region.

**MAIN FOCUS OF RESEARCH**

**STRUCTURE, FUNCTION AND ORGANISATION OF THE DEPARTMENT**

**IMPORTANT PUBLICATIONS | MAX. 5**


**IMPORTANT PROJECTS | MAX. 5**

**Early lumbar drainage after aneurysmatic subarachnoid bleeding: a randomized, clinical study (EARLYDRAIN)**

Project Manager: Dr. T Karz
Cooperation: Neurosurgery, Charité Berlin
Project Duration: 2011 - 2015

**Erythropoietin in SHT: a randomized placebo-controlled study in intensive care patients.**

Project Manager: Dr. T Karz
Cooperation: The Australian & New Zealand Intensive Care Research Centre, School of Public Health and Preventive Medicine, Monash University Melbourne, Australia
Funding: The Australian & New Zealand Intensive Care Research Centre, Department of Epidemiology and Preventive Medicine, School of Public Health, Monash University, Melbourne, Australia
Sum: € 20,000
Project Duration: 2012 - 2015

**Intraventricular hemorrhage trial**

Project Manager: Dr. T Karz
Cooperation: Brain Injury Outcome Center, Johns Hopkins University, Prof. W. Müller-Forell, Institute of Neuroradiology, Prof. K Lackner, Institute of Clinical Chemistry and Laboratory Medicine, Funding: NIH
Sum: € 45,000
Project Duration: 2011 - 2014

**The role of protein kinase C-isozyme 2 in renal cell carcinoma and therapeutic options for kinase-inhibitors in metastatic disease**

Project Manager: Prof. W Brenner
Cooperation: PD Dr. S Walenta, Institute for Physiology and Pathophysiology, Dr. R Unger, Institute of Pathology, PD Dr. J Brünger, Klinikum der Jena and University of Jena
Funding: German Association for Neurosurgery
Sum: € 10,000
Project Duration: 2013 - 2015

**The role of protein kinase C-isozyme 2 in renal cell carcinoma and therapeutic options for kinase-inhibitors in metastatic disease**

Project Manager: Dr. N Keric
Cooperation: PD Dr. J Brieger, HNO et al.
Funding: The Australian & New Zealand Intensive Care Research Centre, School of Public Health and Preventive Medicine, Monash University Melbourne, Australia
Sum: € 45,000
Project Duration: 2012 - 2015

**Urokinase on renal cell carcinoma and therapeutic options for kinase-inhibitors in metastatic disease**

Project Manager: Prof. W Brenner
Cooperation: PD Dr. S Walenta, Institute for Physiology and Pathophysiology, Dr. R Unger, Institute of Pathology, PD Dr. J Brünger, Klinikum der Jena and University of Jena
Funding: German Association for Neurosurgery
Sum: € 10,000
Project Duration: 2013 - 2015

**Erythropoietin in SHT: a randomized placebo-controlled study in intensive care patients.**

Project Manager: Dr. T Karz
Cooperation: The Australian & New Zealand Intensive Care Research Centre, School of Public Health and Preventive Medicine, Monash University Melbourne, Australia
Funding: The Australian & New Zealand Intensive Care Research Centre, Department of Epidemiology and Preventive Medicine, School of Public Health, Monash University, Melbourne, Australia
Sum: € 20,000
Project Duration: 2012 - 2015
The Department of Urology is a tertiary care hospital. Together with our Pediatric Urology Division, which is renowned as one of the largest centers in Germany attracting international patients, we provide complete urological care for all age groups, from birth to the senium. We are able to offer our patients the complete broad spectrum of surgical techniques available for the treatment of malignant tumors of the urogenital tract. Minimal invasive interventions, such as robotic-assisted radical prostatectomy, endoscopic removal of bladder tumors or the laparoscopic removal of renal tumors rank among our standard procedures.

In addition to operative therapy for urological tumors, we also provide medical treatment for all urological tumors in accordance with neoadjuvant, adjuvant and palliative diagnostic evaluations, in both inpatient and outpatient settings. An interdisciplinary continence center, certified through the German Continence Society and under the leadership of the Department of Urology, provides patients with comprehensive treatment and care in cases of benign diseases, such as bladder dysfunction.

The Pediatric Urology Division, led by Prof. Raimund Stein, provides the entire spectrum of diagnostic and therapeutic treatment methods – from the undescended tests to anomalies of the genitourinary tract.

The working group Uro-Oncology is concerned with basic scientific (under the leadership of Dr. Neisius, is the further development of acoustic lens design for electromagnetic lithotripters. This work is carried out in close interdisciplinary collaboration with the Department of Mechanical Engineering and Materials Science of the Duke University in North Carolina, USA. The aim is shockwave morphology at broadest possible focus. Lectures on the new innovative lens design for electromagnetic lithotripters found much international acclaim, which has led to a working cooperation with major investment for the continuation of the projects in progress at our hospital. The first clinical studies on patients involving a new lithotripter are currently being initiated.

The prophylactic medical tumor therapy in primary curatively treated renal cell carcinoma patients with high recurrence risk is also the subject of current research projects (Project “VEG”). Furthermore, this working group is also occupied with the pathogenesis of renal cell carcinoma at a molecular biological level; in particular the development of new more precise signal transduction inhibiting therapies and their resistance building properties, compared to the already established kinase inhibitors. Additionally, the organ specificity of bone metastases of renal cell carcinoma is characterized at a molecular level. With regard to prostate cell carcinoma and bladder carcinoma, a patient-orientated therapy according to the “molecular biological fingerprint”, especially via immunohistochemical techniques is being investigated. The knowledge thus gained will assist in better selection of tumors according to their possible response to chemotherapy or hormonal therapy.

The working group Pediatrics/Reconstruction cooperates with CURE-Net, a network for congenital uro-rectal malformations, that combines the modern principles of genetic and molecular biology, with the purpose of identifying the reasons for congenital deformities of the urogenital tract.

The renal and bladder Stones working group, under the leadership of Prof. Raimund Stein, provides the entire spectrum of diagnostic and therapeutic treatment methods – from the undescended tests to anomalies of the genitourinary tract.

Toxins and carcinomas. The studies examine the active mechanisms of new chemotherapeutics or also focused inhibition therapies in terms of “target therapy”, largely in tumors in locally advanced and metastasized stages (Project “CP15”). The prophylactic medical tumor therapy in primary curatively treated renal cell carcinoma patients with high recurrence risk is also the subject of current research projects (Project “VEG”). Furthermore, this working group is also occupied with the pathogenesis of renal cell carcinoma at a molecular biological level; in particular the development of new more precise signal transduction inhibiting therapies and their resistance building properties, compared to the already established kinase inhibitors. Additionally, the organ specificity of bone metastases of renal cell carcinoma is characterized at a molecular level. With regard to prostate cell carcinoma and bladder carcinoma, a patient-orientated therapy according to the “molecular biological fingerprint”, especially via immunohistochemical techniques is being investigated. The knowledge thus gained will assist in better selection of tumors according to their possible response to chemotherapy or hormonal therapy.

The working group Pediatrics/Reconstruction cooperates with CURE-Net, a network for congenital uro-rectal malformations, that combines the modern principles of genetic and molecular biology, with the purpose of identifying the reasons for congenital deformities of the urogenital tract.

In the case of the bladder extrophy-epispadias complex (BEEK), the group is planning a nationwide prospective longitudinal study to establish reliable prognostic parameters in the new-born phase and outcome-relevant implications of the various treatment modalities (single-stage versus two-stage reconstruction) for postoperative results.

Through a multicenter transversal study including all age groups, this group evaluates the relevance of postoperative long-term complications to achieve an age and gender-suited algorithm for follow-up care, which will consider gender-specific needs and psychosocial aspects. Furthermore, as a member of the research focused BiomaTICS, the group is concerned with the establishment and optimizing of an in vitro generated pre-vascularized buccal mucosa for the reconstruction of the urethra. In this context, there exists a close cooperation with the Departments of Pathology, Otolaryngology, Head and Neck Surgery, Oral and Maxillo-Facial Surgery, the Max Planck Institute for Polymer Research as well as the Institute for Microtechnology in Mainz.

As part of a working cooperation with an ESWL development team, organized by the medical equipment industry, the working group Renal and Bladder Stones (Nephrolithiasis) organizes annual international tutorials and workshops on the practical attributes of shock wave lithotripsy for kidney stone fragmentation. A key aspect of the working group, under the leadership of Dr. Neisius, is the further development of acoustic lens design for electromagnetic lithotripters. This work is carried out in close interdisciplinary collaboration with the Department of Mechanical Engineering and Materials Science of the Duke University in North Carolina, USA. The aim is shockwave morphology at broadest possible focus. Lectures on the new innovative lens design for electromagnetic lithotripters found much international acclaim, which has led to a working cooperation with major investment for the continuation of the projects in progress at our hospital. The first clinical studies on patients involving a new lithotripter are currently being initiated.
Department of Anesthesiology

Mainz University Medical Center’s Department of Anesthesiology covers the full spectrum of scientific and clinical anesthesiology. Clinical anesthesia, critical care medicine, pain therapy, preclinical emergency medicine and palliative care. 27,000 patients receive general or regional anesthesia or a combination of both in a total of 37 OR’s. The Department’s critical care unit is the primary ICU in the state with expertise for treatment of all surgical and common internal medicine diseases. All treatment options to care for patients with multiple organ failure are available. The department’s special interest to care for patients with acute respiratory distress syndrome is well known beyond state limits, resulting in acquisition of patients with ARDS from several German states. Preclinical emergency medicine is performed by staffing two physician-led emergency medicine ambulance trucks, taking care of approximately 5800 patients annually. In addition, the emergency medicine helicopter “Christoph 77” is manned by the department, taking care of more than 1400 severely distressed patients per year. Within the hospital, a specialized physician-led “Medical Emergency Team (MET)” is available for all persons requiring immediate resuscitation – consequently, 900 patients per year receive urgently needed care within a proper time frame. Pain therapy consists of a division of acute pain therapy, and a division of chronic pain disease, respectively, serving approximately 4000 patients each year in an interdisciplinary cooperation. In Mainz, palliative care makes the fifth column of the Department of Anesthesiology, responsibility for these patients is shared with the Department of Hematology and Oncology and the Department of Neurology.

Fig. 93: Anesthesiology workstation in the OR.

Fig. 94: Interdisciplinary emergency trauma room training.

Basic Science Key Research Groups

Traumatic brain injury
Research is focused on pathophysiologival mechanisms and therapeutic options following traumatic brain injury.

Pulmonary pathophysiologival
To investigate basic mechanisms and therapeutic options in isolated lung injury and lung sepsis models. Additionally, cyclic oscillations of oxygen pressure due to shear stress are studied to elucidate their effect as a mediator of neuronal lesion.

Resuscitation
This project studies cerebral microperfusion during resuscitation using state-of-the-art monitoring and MR-based imaging technology.

Biopsychosocial factors
Having established a simple screening test to describe biopsychosocial predictors, the focus of this project is to study the impact of biopsychosocial factors on patients' outcome.

IMPORTANT PROJECTS | MAX. 5

Evaluation of drug management of the medical task force concept during simulation of medical catastrophes
Project Manager: Prof. H. Gevao, Dr. H. Buggenhagen
Funding: Federal Office of Civil Protection and Disaster Management (BBK)
Sum: € 433,894
Project Duration: 2012 - 2014

Functional Role of the Proteasome and Autophagic Protein Degradation System in Neuronal Homeostasis Following Traumatic Brain Injury (SP 467) - CRC 1080/1 - "Molecular and Cellular Mechanisms of Neuronal Homeostasis"
Project Manager: Prof. C. Baehni, Prof. K. Engigold, Prof. T. Mittmann
Cooperation: Prof. K. Engigold, Department of Anesthesiology, Prof. T. Mittmann, Institute of Physiology
Funding: German Research Foundation / CRC
Sum: € 442,400
Project Duration: 2013 - 2016

Investigation of the causal contribution of the selective glucose transport via the blood brain barrier in the formation of brain edema and neurocognitive disorders after experimental focal cerebral ischemia and head trauma
Project Manager: PD Dr. S. Thal
Cooperation: Prof. C. Förster, University Würzburg
Funding: German Research Foundation
Project Duration: 2010 - 2013

Molecular Mechanisms and Neuronal Homeostasis during Inflammatory Processes in the CNS (CRC1080)
Project Manager: Prof. M. Schäfer, Prof. F. Zipp
Funding: German Research Foundation
Sum: € 449,600
Project Duration: 2013 - 2016

Pathomechanistic Analysis of Mutations in the Cell Adhesion and Recognition Molecule L1CAM
Project Manager: Prof. M. Schäfer
Funding: German Research Foundation
Sum: € 208,692
Project Duration: 2011 - 2014
Clinical Institutes and Departments

- Neuropathology
- Institute of Human Genetics
- Institute of Clinical Chemistry and Laboratory Medicine
- Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI)
- Neurosurgical Pathophysiology
- Institute of Neuroradiology
- Institute of Pathology
- Institute of Molecular Medicine
- Department of Diagnostic and Interventional Radiology
- Department of Nuclear Medicine
- Department of Radiation Oncology and Radiation Therapy
Neuropathology

The Neuropathology at the University Medical Center of the Johannes Gutenberg University in Mainz covers the complete spectrum of diagnostic services in neuropathology, not only applying histological techniques, enzyme histochemistry, immunohistochemistry and electron microscopy, but also adopting molecular methods for the diagnosis of biopsies concerning the central and peripheral nervous systems and skeletal muscle. Furthermore, our diagnostic spectrum includes cytochemical diagnosis of cerebrospinal fluid. Apart from biopsy examinations, we are also responsible for brain autopsies for Mainz University Medical Center and affiliated Academic Teaching Hospitals.

The diagnostic focus is on the classification of brain tumors which is increasingly based on molecular genetics. Furthermore, we are specialized in the diagnosis of neuromuscular diseases. In particular for the diagnostic clarification of mitochondrial diseases, we closely collaborate with molecular experts of the Institute of Clinical Chemistry and Molecular Diagnostics, headed by Prof. Bauer at Ludwigshafen Medical Center, a Teaching Hospital of the Johannes Gutenberg University in Mainz.

The Neuropathology at the University Medical Center of the Johannes Gutenberg University in Mainz is the only institution in Rhineland-Palatinate which offers complete recognized postgraduate medical-specialist education for residents in the specialist field of neuropathology to become certified neuropathologists.

Important Publications

- Fraunhofer K, Katzav A, Grimm C et al. (2013; 218 (4): 517-526). Neurological impairment in experimental antiphospholipid syndrome is associated with increased ligand binding to hippocampal and cortical serotonin 5-HT1A receptors. IMMUNOBIOLOGY.
- Zaydut M, El Mahi K, Fraunhofer K et al. (2013; 218 (4): 1037-1047). Subclinical CNS Inflammation as Response to a Myelin Antigen in Humanized Mice. JOURNAL OF NEUROIMMUNE PHARMACOLOGY.
The Institute of Human Genetics is the leading institution of that kind in Rhineland-Palatinate and the metropolitan Rhine-Main area, which covers 5.6 million inhabitants. We are responsible for the counseling, diagnostics and management of patients with a large variety of genetic disorders with a special focus on rare diseases and/or severe forms of disease.

In our laboratories we carry out a large spectrum of cytogenetic, molecular cytogenetic and molecular genetic diagnostics including epigenetic and other up-to-date methods. We are specialized in patients with developmental delay and intellectual disability, behavioural problems including autism spectrum disorder, epilepsy and hearing loss. In addition we have built up a Huntington’s Disease research and treatment center for the care of patients with Huntington’s Disease and similar neurodegenerative disorders.

**STRUCTURE, FUNCTION AND ORGANISATION OF THE INSTITUTE**

Human genetics is a bridge discipline between life sciences and medicine. With growing knowledge about gene defects as a basis for genetic diseases and the increasing understanding of the biochemical pathways associated with these genes, new possibilities of therapy development for genetic diseases have evolved. The Institute is embedded into in the Research Center for Translational Neurosciences (FTN) of the Johannes Gutenberg-University Mainz, which together with our clinical orientation focusing on genetic diseases of the central nervous system allows us to bridge between patient care and basic research and between gene discovery and therapy development together with experts of different disciplines.

**MAIN FOCUS OF RESEARCH**

Many functions of the healthy brain are regulated by local protein synthesis. Thus, the so-called synaptic plasticity representing the biology basis of learning and memory depends on the well-functioning and fine-tuned protein biosynthesis in the dendrites, axons and in particular the postsynaptic compartment. Deregressed local protein synthesis leads to diseases like fragile X syndrome, Down syndrome and Rett syndrome. Similarly, deregulated local protein synthesis in neurons is critically involved in the pathogenesis of neurodegenerative diseases, especially Huntington’s Disease. By studying patients with a rare genetic disease, the so-called Opitz BB/G syndrome, this mechanism is defective, PP2a activity is enriched at the microtubules and microtubule-associated proteins are hypophosphorylated (Nature genetics, 2001).

**Fig. 97:** The ubiquitin ligase MID1 targets microtubule-associated PP2A towards ubiquitin specific degradation by the proteasome. In patients with Opitz BB/G syndrome this mechanism is defected, PP2A activity is enriched at the microtubules and microtubule-associated proteins are hypophosphorylated (Nature genetics, 2001).

**Fig. 98:** The ubiquitin ligase MID1 targets PP2A towards ubiquitin specific degradation by the proteasome. At the same time mTOR activity increases and protein translation of an mRNA containing an expanded CAG repeat is initiated (Nature communications, 2013).

**Fig. 99:** Dysregulated mTOR activity is a main reason for hereditary forms of intellectual disability.

**IMPORTANT PROJECTS | MAX. 5**

**Characterization of putative pluripotency-regulating genes and defining the role of germ cell-specific genes during reprogramming**

Project Manager: PD Dr. U Zechner

Cooperation: Dr. J Nolte, Department of Human Genetics, University Medical Center Göttingen, Prof. W Engil, Department of Human Genetics, University Medical Center Göttingen

Funding: German Research Foundation

Sum: € 178,275

Project Duration: 2011 - 2014

**Spermatogonial stem cells and their potential**

Project Manager: PD Dr. U Zechner

Cooperation: Prof. W Engil, Georg-August University Göttingen, Institute for Human Genetics, Dr. J Nolte, Georg-August University Göttingen, Institute for Human Genetics, Prof. W Schulze, Abteilung Andrologie, University Hamburg Eppendorf

Funding: German Research Foundation

Sum: € 130,950

Project Duration: 2011 - 2014
The research activities of the Institute are focused mainly on the pathogenesis of arteriosclerosis and thrombosis. There are several research groups which use in vitro and in vivo models as well as clinical and epidemiologic approaches to elucidate the underlying mechanisms of these disorders. Within these activities the Institute is integrated in several research clusters of the University Medical Center, e.g. the Center for Thrombosis and Hemostasis (CTH), the Gutenberg Health Study (GHS), and the Center for Translational Vascular Biology. With the implementation of the professorship for experimental hemostasis within the CTH in December 2012 held by Prof. O Bartsch, Institute of Human Genetics et al. (Helmholtz-Center Munich), study of Health Genetics et al. (Max. 6).

The Institute is involved in the development, improvement, validation, and quality control of clinical laboratory diagnostics which is today one of the largest centers in Germany caring for patients with endothelial and platelet dysfunction. Besides these central research foci the Institute is involved in the development of new test systems. Research on the pathogenesis of thrombotic events concentrates on the most common acquired thrombophilias, the antiphospholipid syndrome. While this autoimmunologic disorder is a core competency of our specialty, the Institute is a reference laboratory for cerebro-spinal fluid testing of the Reference Institute for Bioanalytics of the German Society of Clinical Chemistry and Laboratory Medicine. Development of laboratory diagnostics in the Institute applies to many different fields of laboratory medicine, but is focused again on cardio-vascular diagnostics, hemostasesology, and molecular diagnostics. In particular in the latter area we develop novel diagnostic approaches to complex diseases such as von Willebrand disease, hemoglobinopathies, and endocrine tumor syndromes. In particular, the field of endocrine tumors has grown from a cooperation between the Institute, the endocrinology branch of the I. Dept. of Medicine and the Dept. of Surgery into a joint effort of several institutions of the University Medical Center, which is today one of the largest centers in Germany caring for patients with endocrine tumors. Besides its own interests in research and development, the Institute supports a large number of clinical studies with the required laboratory tests. This also includes testing of blood samples from animal studies, which often times require special test procedures.
Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI)

STRUCTURE, FUNCTION AND ORGANISATION OF THE INSTITUTE

The Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI) was founded in 1943 and is tasked with supporting clinical research with methodological expertise, conducting in-house methodological research and representing the profession at the University Medical Center Mainz through research and teaching. Currently the IMBEI consists of four divisions: biostatistics, epidemiology, informatics and documentation. Two cancer registries are located at the IMBEI: the German Childhood Cancer Registry and the Rhine Land Palatinate Cancer Registry.

The IMBEI’s goal is to contribute to sustaining and improving the health of the general public and patients through its expertise in the areas of biostatistics, epidemiology, informatics and documentation. Scientific advance is only achievable with appropriate methods. Therefore, our main objective is to support medical research with our diverse methodical expertise.

One of the main tasks of the Division Bioinformatics is providing statistical support for research projects at the University Medical Center Mainz. The methods research of the division focuses on planning and evaluation of studies, in particular in the area of personalized medicine with high-dimensional molecular data. A further focus is on methods for the use of clinical registries and secondary data. For performing studies, we work closely together with clinical departments and the IZKs, and we offer a bioinformatics support interface via the Core Facility Bioinformatics (BIuM-MZ).

Epidemiologists at the IMBEI conduct population-based observational studies in the areas of radiation epidemiology, health services research and pediatric epidemiology. The focus for radiation epidemiology is one the health consequences of occupational radiation exposure at low doses (for example, nuclear plant employees) and the outcomes of medical diagnostic use (for example, CT examinations). In the area of therapeutic use of ionizing radiation, possible outcomes concerning cardiovascular diseases are examined in addition to possible cancer endpoints. The Division of Epidemiology and Health Services Research investigates the effects of diseases and health care on quality of life and mental health in patients with chronic diseases, the interplay of societal factors and health, and life course epidemiology. Other areas of interest are prevention of malignant diseases, occupational health risks, and evidence based medicine. The Division of Pediatric Epidemiology at IMBEI is investigating the health effects of transition from early childhood into school age and the impact of chronic diseases on school performance and academic achievement in children.

The Division of Medical Informatics is involved in three areas: “IT for collaborative research”, “IT innovation at the hospital” and “telehealth”. Under these headings are topics such as distributed systems, decentralized search algorithms for collaborative searching that maintain the data sove- rainty of a centre, the use of mobile devices and Web 2.0 applications in patient-doctor interactions, the analysis and development of clinical documentation systems, establishing interoperability in the data and process levels, and empowering patients and citizens to actively take part in the data streams that affect them. Tasks and research related to data protection and data security have been a major area of action for IMBEI for years. In addition to scientific concepts, the department is also involved with user-ready software implementations for our partners. Complex cooperation networks and studies are also incorporated into configurable clinical registries. The support of rare disease research networks also distinguishes the IMBEI: the nation-wide German Childhood Cancer Registry and the Rhine Land Palatinate Cancer Registry.

The Medical Documentation Division’s main focus is on data management in epidemiological and biometrical studies. Data management includes the complete spectrum, beginning with study planning and continuing on to database development and programming the evaluation routines. Two cancer registries are located at the IMBEI: the nation-wide German Childhood Cancer Registry and the Rhine Land Pa- latinate Cancer Registry with its registration office. In epidemiological cancer registries, basic epidemiological data (for example, age, sex, diagnosis, localization, residence, type of diagnosis confirmation, death infor- mation) on the population in a defined region are collected. In this way, it is possible to determine diagnosis-specific and age-specific incidence rates and changes in incidence over time as well as to identify regional clusters and calculate survival probabilities.

MAIN FOCUS OF RESEARCH

The IMBEI consists of four divisions:

1. Biostatistics
2. Epidemiology
3. Informatics
4. Documentation

Each division has its own specific research focus and collaborates closely with clinical departments and research networks. The department is responsible for the courses “Biostatistics for Clinical Scientists”, “Epidemiology and Biostatistics”, “Medical Informatics and Biostatistics”, and “Evidence-Based Medicine – How Knowledge is Generated”. In addition, the IMBEI offers a post-graduate and consecutive program leading to a master’s degree in epidemiology (M.Sc.).

An interdisciplinary team of about 90 dedicated employees works at the IMBEI. The IMBEI is integrated into the methodological training of students of human medicine and is responsible for the courses “Biome- try, Informatics and Epidemiology” and “Epidemiology and Biostatistics for Clinical Scientists”.

IMBEI Core Facility Bioinformatics

The Core Facility Bioinformatics (BIuM-MZ) is an important project with a large number of research projects coordinated by the IMBEI. The main focus of the Core Facility is the management of data in national and international scientific research projects. The data management includes the complete data management, beginning with study planning and continuing on to database development and programming the evaluation routines. Two cancer registries are located at the IMBEI: the nation-wide German Childhood Cancer Registry and the Rhine Land Palatinate Cancer Registry with its registration office. In epidemiological cancer registries, basic epidemiological data (for example, age, sex, diagnosis, localization, residence, type of diagnosis confirmation, death information) on the population in a defined region are collected. In this way, it is possible to determine diagnosis-specific and age-specific incidence rates and changes in incidence over time as well as to identify regional clusters and calculate survival probabilities.

### IMPORTANT PROJECTS | MAX. 5


Neurosurgical Pathophysiology

The institute was founded in 1990 with the aim to provide high quality research for clinical partners. It is equipped with operating rooms for small and large animals, labs for serial sections and immunohistochemistry, conventional and confocal microscopes, a cell culture lab etc. We focus on cooperations with clinical partners and have our own dedicated projects.

MAIN FOCUS OF RESEARCH

Activities cover two objectives

1. Topics of interests covered by institute members since many years: Pathophysiology of severe head injury, subdural (intracerebral) bleeding, focal and global cerebral ischemia, and

2. Topics initiated by internal/external cooperations: ultrasound hemolysis, testing of intracranial materials and instruments (nanocarbon electrodes, new multiparametric sensors, establishment of a ‘blood-brain barrier on a chip’ in-vitro etc.)
In the federal state of Rhineland-Palatinate, the Institute of Neuroradiology is the only university department that provides complete diagnostic and therapeutic neuroradiological assessment throughout the year (24h/7days/365days). During 2013, in excess of 9.500 CT, approximately 4.000 MRI (including fMRI, spectroscopy and perfusion) 500 angiographies including therapeutic interventional procedures were carried out. The latter include: Emergency examinations of neurosurgical patients presenting with life-threatening hemorrhages of ruptured aneurysms of the cerebral arteries (so called coiling of aneurysms).

Emergency mechanical recanalization (thrombectomy) in stroke patients, patients from the stroke unit (1.order), in the Clinic of Neuroradiology of the University Medicine Mainz.

Arterial embolisation of cerebral and spiral arteriovenous malformations (AVM) and arteriovenous fistulate (AVF), preoperative tumor-embolisation and therapy of intractable epilepsy (mainly in emergency).

Stent-application of extra- and intracranial arteries in order to prevent recurrent stroke. This therapy is especially crucial in case of failure of conservative drug assisted therapy.

In conjunction with other clinics, functional MRI (fMRI) and imaging of disease of the visual pathway are the main focus of the research.

In co-operation with the Clinic of Psychiatry, the diameter of the basal artery is evaluated using MR-angiography in a collective of healthy children and adults. This serves as a reference to young patients suffering from M Fabry, as it is not known which age the dilation of the basal artery develops.

Another focus (in co-operation with Prof. Kalsch, Director of the Neuromaging Center (NIC) of the FTN) is functional MRI using spatially presented memory paradigms, as well as diffusion-tensor-imaging (DTI) in patients with early stage Alzheimer disease. Additionally the database contains standard as well as DTI- and susceptibility-weighted images of healthy elderly people in order to have a reference-collective for investigation of cerebral dysfunction in dementia patients.

In another interdisciplinary project, functional MRI is performed in order to investigate neuronal correlates of emotional processing in hypnotic induced and clinical depersonalization. Patients with severe depersonalization are matched with a corresponding collective of patients, with patients with severe anxiety and depression and a group of healthy people.

A further study, performed together with the Clinic of Psychosomatic Medicine and Psychotherapy, investigates the impact of multimodal stationary acute therapy on the capacity of mentalisation using fMRI and is evaluated in patients with somatisation dysfunction. We want to know if there is a difference in performance and functional neuromaturation in mentalisation processes between the patients and a (concerning age, gender, and educational background) matched control group of healthy people. Additionally we wish to research whether or not a group multimodal psychotherapy over 8 to 12 weeks in a stationary environment, focused on patients with somatization dysfunction, will lead to a better mentalisation capacity.

Together with other groups (i.a. ophthalmology, rheumatology, neurosurgery) we study a reliable biopsy planning in patients with giant cell arteritis. The basic data of high resolution imaging of the temporal artery are directly transmitted in a neurosurgical navigation system, focused on patients with giant cell arteritis. The basic data of high resolution imaging of the temporal artery are directly transmitted in a neurosurgical navigation system.


MR research on small animals is also carried out in conjunction with interdisciplinary groups e.g. anaesthesiology, nuclear medicine and neurosurgery.

Field-study: a randomized, multicenter, multinational, phase 3b, open-label, parallel-group study to evaluate the efficacy and safety of ocrexinumab in comparison to interferon beta-1a (Rebiot) in patients with relapsing Multiple Sclerosis. Project Manager: Prof. F. Zipp, Dr. J. Schadam-Fischer, PD Dr. AP Barreno-Ciara et al. Project Duration: 2011 - 2014

A randomized, double-blind, double-dummy, parallel-group study to evaluate the efficacy and safety of ocrelizumab in patients with relapsing Multiple Sclerosis. Project Manager: Prof. F. Zipp, Prof. W. Mueller-Forell. Project Duration: 2012 - 2014

Distribution and concentration of ferritin in cortical and subcortical brain parenchyma and its age- and gender correlation.

Project Manager: G. Vucurovic, Dr. J. Gawehn Project Duration: 2012 - 2014

Institute of Neuroradiology

**STRUCTURE, FUNCTION AND ORGANISATION OF THE INSTITUTE**

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Stent-application of extra- and intracranial arteries in order to prevent recurrent stroke. This therapy is especially crucial in case of failure of conservative drug assisted therapy.

**MAIN FOCUS OF RESEARCH**

A multi-center double-blind parallel-group placebo-controlled study of the efficacy and safety of teriflulomide in patients with relapsing Multiple Sclerosis who are treated with interferon-beta.

Project Manager: Prof. F. Zipp, Dr. J. Schadam-Fischer, PD Dr. AP Barreno-Ciara et al.

Project Duration: 2011 - 2014

A randomized, double-blind, double-dummy, parallel-group study to evaluate the efficacy and safety of ocrelixumab in comparison to interferon beta-1a (Rebiot) in patients with relapsing Multiple Sclerosis.

Project Manager: Prof. F. Zipp, Prof. W. Mueller-Forell.

Project Duration: 2012 - 2014

Distribution and concentration of ferritin in cortical and subcortical brain parenchyma and its age- and gender correlation.

Project Manager: G. Vucurovic, Dr. J. Gawehn

Project Duration: 2012 - 2014

**IMPORTAND PROJECTS | MAX. 5**

**Schroeder JC, Lassig AK, Galetzka D et al.**

A boy with homozygous microdeletion of NEUROG1 presents with a congenital cranial dysinnervation disorder (Moebius syndrome variant).

**BEHAVIORAL AND ORGANISATION OF THE INSTITUTE**

**Professor Wibke s. müller-Forell**

**Acting Director:**

**Professor Wibke S. Müller-Forell**

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The Institute of Pathology provides central service for histo-pathological, cytological, molecular-pathological and ultrastructural diagnosis for the University Medical Centre Mainz. Actually, in the Institute specimens of more than 60,000 patients are studied annually. Beneath the classical methods of histological, cytological, immunohistological and immunocytochemical analyses, which are all performed in an automated standardized manner, the institute provide modern methods in molecular biological techniques including Laser Capture Microdissection. Furthermore, the Institute of Pathology provides the only complete electron microscopic laboratory at the clinic campus for both transmission and scanning electron microscopy with the possibility for ultrastructural tomography. In this context, in 2012 a new transmission electron microscope with a high-resolution digital camera was installed based on co-funding of the German Research Foundation (DFG) and the state government. Since 2007, the Institute of Pathology in Mainz has been accredited. Thus, we ensure for all our patients, our referring physicians and our research partners for high quality of diagnoses and analyses. By that we serve for collaboration in clinical and transnational research with various national and international clinical partners. Actually, we established a Tissue-biobank based on a fully automated robotic system for tissue assurances at -196°C (SmartFreezer®) enriched with a dynamic monitoring system and automatic alert-system. Furthermore, we combined the biobank-data management system with other data bases such as the hospital information system, the management system of the laboratory chemistry and in near future with the clinical tumour documentation system to provide high quality, data rich specimens.

**MAIN FOCUS OF RESEARCH**

The REPAIR-lab represents the research laboratory of the institute, which use scientific approaches to study cell and tissue interaction with biomaterials. The REPAIR-lab is one of the founding laboratories in the European Commission Network of Excellence EXPERTTISSUES, now the European Institute of Excellence on Tissue Engineering & Regenerative Medicine. The German Federal Ministry of Education and Research (BMBF) awarded the REPAIR-lab funding for a German-Chinese Young Investigator Group in Regenerative Medicine for 5 years (2007-2012). The research team has also been part of two major Priority Programmes of the German Research Foundation (DFG), namely SPP1100: Interface between material and tissue engineering, and SPP1131: Biomedical responses to nanoscale particles: “Bio-Nano-Responses” (2008-2013).

The Institute is focussed on the following:

- **in vitro models of biological vascu-larization**
  - The REPAIR-lab has established quantifiable in vitro models to understand how various factors modulate this essential biological reaction, especially in the context of biomaterials and tissue engineering. We are using a number of human endothelial cell types, both primary and in the form of permanent cell lines, to investigate various research questions on endothelial function and vascular growth. Endothelial function is studied using state-of-the-art cell and molecular biological methods.
  - In vitro models for bone tissue engineering
    - It has become apparent that bone growth is dependent on adequate vascularization, which is a focus of our research. In our in vitro approach, we investigate how osteoblasts interact with endothelial cells, with the aim to better understanding of the regenerative process. Co-culture systems have been established and used within the scope of two European projects (AUTOBone & HIPPOCrates).
  - In vitro studies on human adult stem cells
    - We are isolating endothelial progenitor cells (EPCs) from human peripheral blood with a view to unravelling the steps in line age differentiation, their interactions with three-dimensional scaffolds and matrices for tissue engineering, as well as their possible integration into local microcirculation networks. More recently, in the scope of an EU project to tissue engineer an intervertebral disc (Disc Regeneration, 2008-2012) human mesenchymal stem cell cultures were set up.
  - In vitro models for NanoMedicine
    - The development of the field of Nanomedicine involves various concepts such as targeted drug- and gene delivery using engineered nanoparticles. Relevant portals of entry are the air-blood barrier (ABB) or the blood-brain-barrier (BBB). We have spent many years setting up functional co-culture systems using state-of-the-art cell and molecular biological methods.
  - In vitro models for respiratory tract regeneration
    - Since many years we have set up stable cultures of human cells to simulate the upper and lower respiratory tracts. The former can be established in vitro using cocultures of respiratory progenitor cells and fibroblasts, while the latter demands so-called type I alveolar epithelial cells with microvascular endothelial cells. These coculture models have been used to study how cellular crosstalk between the different cell types is involved in maintaining the integrity of both the upper and lower respiratory tract. This knowledge is a pre-requisite for rational approaches to generate the tracheo-bronchial system and the lung parenchyma, especially the alveolo-capillary system.
Institute of Molecular Medicine

The Institute for Molecular Medicine (IMM) is a basic research institute working with many methods in molecular and cellular biology and different immunological methods. In addition, it serves as a template for mouse genetics and assists different laboratories in the University Medical Center of Mainz in the generation of mouse mutants. The IMM takes part in different national and international collaborative grants, financed mostly by the German Research Foundation (DFG) and in addition by other national and European agencies. In addition, the IMM takes part in the local immunological consortia, Research Center Immunology (TZI) funded by the Land of Rhineland-Palatinate. The IMM also participates in national transregional centers funded by the DFG or the Federal Ministry of Education and Research (BMBF). Prof. Ari Waisman has been the director of the IMM since 2010. It has since then increased its staff up to 40 people. The institute is composed of 5 research groups that are headed by two professors, Prof. Ari Waisman and Prof. Björn Clausen who joined from Rotterdam recently. The other 3 groups are headed by Dr. Nadine Hövelmeyer, Dr. Simone Wörgle and Prof. Florian Krummbach. In addition to the group leaders, the institute staff is composed of 6 postdocs, 8 phd students, 8 technicians along with various medical students, masters and bachelor students as well as two secretaries and kitchen staff from a very international team. 50 % of the scientists in the IMM are women. Each year the IMM hosts students in different levels who participate in a practical period („Praktikum“). In recent years this included master students spending 4-6 weeks in the lab as well as visiting students from Africa and South America. As from the current academic year the Institute is coordinating the Master program in Biomedicine.

The research focus of the Institute for Molecular Medicine (IMM) is the study of basic mechanisms of inflammatory diseases. We focus on autoimmune diseases such as multiple sclerosis (MS) as well as other diseases that affect the gut, skin and heart. In addition to inflammatory/autoimmune diseases, our institute is also interested in basic mechanisms that control the function of the immune system, including signal transduction pathways, primary investigating molecules that control the activation of the nuclear factor kappa B (NFκB) transcription factors, in their involvement in malignant diseases. The immune system contains two arms, the innate and adaptive arm. We aim to gain a better understanding how T cells, which belong to the adaptive immune system trigger autoimmune diseases, and how they influence also the involvement of innate immune cells in these diseases. For example, we study T cells, which produce IL-17, and are termed Th17 cells. Secrecy of IL-17 results in a chain of events that leads to the infiltrations of neutrophils to the sites of inflammation. Much of the research in the IMM involves genetically manipulated animals. We use a technology termed conditional gene targeting, to generate mice that lack certain genes, or overexpress certain genes, in specific cells types. Using the example from above, we generated mice that overexpress IL-17 and we now study how this influences autoimmunity. Similarly, we generated mice, which lack the gene coding for the IL-17 receptor, to study how the inability of these cells to respond to IL-17 influences autoimmunity. Using the same technology we also investigated g protein-mediated signaling in immune cells: implications for neuroinflammation. The Institute for Molecular Medicine (IMM) is a basic research institute working with many methods in molecular and cellular biology and different immunological methods. In addition, it serves as a template for mouse genetics and assists different laboratories in the University Medical Center of Mainz in the generation of mouse mutants. The IMM takes part in different national and international collaborative grants, financed mostly by the German Research Foundation (DFG) and in addition by other national and European agencies. In addition, the IMM takes part in the local immunological consortia, Research Center Immunology (TZI) funded by the Land of Rhineland-Palatinate. The IMM also participates in national transregional centers funded by the DFG or the Federal Ministry of Education and Research (BMBF). Prof. Ari Waisman has been the director of the IMM since 2010. It has since then increased its staff up to 40 people. The institute is composed of 5 research groups that are headed by two professors, Prof. Ari Waisman and Prof. Björn Clausen who joined from Rotterdam recently. The other 3 groups are headed by Dr. Nadine Hövelmeyer, Dr. Simone Wörgle and Prof. Florian Krummbach. In addition to the group leaders, the institute staff is composed of 6 postdocs, 8 phd students, 8 technicians along with various medical students, masters and bachelor students as well as two secretaries and kitchen staff from a very international team. 50 % of the scientists in the IMM are women. Each year the IMM hosts students in different levels who participate in a practical period („Praktikum“). In recent years this included master students spending 4-6 weeks in the lab as well as visiting students from Africa and South America. As from the current academic year the Institute is coordinating the Master program in Biomedicine.
Department of Diagnostic and Interventional Radiology

**STRUCTURE, FUNCTION AND ORGANISATION OF THE DEPARTMENT**

Radiology is a medical specialty that employs the clinical and scientific use of imaging methods to both diagnose and treat disease.

Fields of activity of the clinic for diagnostic and interventional radiology:

- Diagnostic methods (all acquired image data are in digital format)
  - Radiography (Conventional Radiology)
  - Radioscopy (Fluoroscopy)
  - Computed Tomography (256-slice CT)
  - Magnetic Resonance Imaging (1.5 Tesla - 3.0 Tesla), Non-proton MRI (Helium-3, deuterium gases)
  - Digital Subtraction Angiography (DSA)
  - Sonography
  - Mammaryography

Therapy methods (full spectrum of Interventional Radiology care):

- Balloon dilatation and stent implantaion
- Occlusion of blood vessels
- Percutaneous tumor ablation
- Biliary tract interventions
- Biopsies and marking methods
- Percutaneous drainages

Patients treated with methods of interventional radiology which require in-patient monitoring are taken care in the ward of the Department of Diagnostic and Interventional Radiology (which is used together with the Department of Radiooncology).

**General responsibilities and specialties:**

- Radiology Information System (Database since 1988)
- Picture- Archiving and Communication System (PACS) (Database since 1998)
- Teleradiology
- Clinical Trial Center Radiology
- Section of Medical Physics
- Section of Pediatric Radiology

**MAIN FOCUS OF RESEARCH**

Areas of research:

- Lung imaging using MRI and CT
- Interventional vascular and tumor therapy
- IT and image post-processing in radiology
- Innovative MRI techniques

**IMPORTANT PROJECTS | MAX. 5**

- **Detection of pulmonary hemodynamics in probands with patients with pulmonary hypertension using high-resolution phase contrast MRI (MAIFOR)**
  - Project Manager: Dr. G. Wirth
  - Cooperation: Prof. S. Konstantinides, CTH, Mainz
  - Funding: MAIFOR Project, University Medical Center Mainz
  - Sum: € 50,000
  - Project Duration: 2013 - 2015

- **Dynamic contrast enhanced-MRI in rectal cancer: Inter- and intraobserver reproducibility and the effect of slice selection on pharmacokinetic analysis**
  - Project Manager: Dr. A. Hoetker
  - Project Duration: 2010 - 2013

- **Evaluation of thyroid diseases in pediatric oncological patients after treatment with a high dosage of chemotherapy and/or radiation therapy of the head and neck**
  - Project Manager: Prof. G. Staatz
  - Cooperation: Prof. J. Faber, Center for Childhood and Adolescent Medicine
  - Project Duration: 2013 - 2014

**IMPORTANT PUBLICATIONS | MAX. 5**

Department of Nuclear Medicine

STRUCTURE, FUNCTION AND ORGANISATION OF THE DEPARTMENT

The Department of Nuclear Medicine provides all available diagnostic and therapeutic applications with radiopharmaceuticals. One main clinical focus is the diagnosis and treatment of benign and malignant thyroid diseases (radioiodine treatment), whereas a second focus is the radioprobe therapy of neuroendocrine tumors. The required follow-up examinations are also done by our clinic. Coordination and discussion of complex, interdisciplinary treatment concepts are taking place in a regularly scheduled tumor board in cooperation with specialists from various areas of expertise.

The isotope therapies with a variety of radiopharmaceuticals are performed in our specialized therapy ward with a total of eight beds. Approximately 600 patients per year were admitted to the ward with a mean duration of stay of 3.8 days. About 20% of these patients undergo special (non-radioiodine) therapies with complex radiopharmaceuticals.

The focus here are the following applications:
- Selective Internal Radiation Therapy (SIRT) for malignant diseases of the liver
- Peptide radioreceptor therapy in metastatic neuroendocrine tumors (NET)
- MIBG therapy in neuroblastoma and metastatic pheochromocytoma
- Radiotherapy in metastatic prostate cancer

The Department of Nuclear Medicine performs over 5000 examinations per annum; hence about 1200 PET-CT examinations with various radiopharmaceuticals. Almost 60% of these PET-CTs are performed with F-18-fluorodeoxyglucose (FDG), approximately 20% with Gallium-DOTATOC.

The operation of the PET-CT is carried out together with the Department of Diagnostic and Interventional Radiology. In meetings each examination result will be seen and discussed by specialists of these departments.

The Department of Nuclear Medicine cooperates with the certified Breast Center, the Skin Cancer Center and the “Interdisciplinary Endocrine and Neuroendocrine Tumor Center” (IEEnet).

MAIN FOCUS OF RESEARCH

The current research projects of our neuro nuclear medicine group, which is part of the Focus Program Translational Neuroscience (FTN), are focused on two main aspects:
- The functional relationship between the opioidergic neurotransmission and the dopaminergic reward system in experimental alcohol challenge and addiction.
- The role of the endocannabinoid system in impulsivity using dedicated animal models and (subsequently) experimental challenges in healthy volunteers.

These interdisciplinary investigations are performed by means of PET/CT, animal PET and animal PET/MR. The radiotracers used are synthesized in our radiochemical lab as well as in collaborating external laboratories.

In the field of oncology a main focus of clinical research is the evaluation of efficacy and toxicity of LuTate Therapy (SRT) in neuroendocrine tumors. The clinic is participating in an international multicenter trial (Netter1) and a German registry network. Additionally, retrospective analyses from patients treated at the ENETS Center Mainz are conducted. For example the clinical value of F-DOPA PET/CT as an imaging screening modality for asymptomatic patients from family members with paranganglioma syndromes carrying an SDHx mutation was investigated.

Preclinical research has a main focus on investigation of targeted internal therapy with alpha- and beta emitting isotopes and its radiobiology in vivo and vitro.

IMPORTANT PROJECTS | MAX. 5

**Opioidergic modulation of alcohol action on the dopaminergic reward system**
- Project Manager: PD Dr. C Feil
- Prof. M Schreckenberger
- Cooperation: Department of Psychiatry and Psychotherapy, RWTH Aachen
- Funding: German Research Foundation Sum.: € 230,000
- Project Duration: 2011 - 2014

**The endocannabinoid system and impulsivity: Investigations on the cerebral CB1-receptor status in normal and disturbed impulsivity**
- Project Manager: Prof. M Schreckenberger, Dr. I Miederer
- Project Duration: 2012 - 2014

**Project Duration:** 2011 - 2014

**Glucose metabolism as marker of the activated immune system**

**Mechanism of impulse control: Imaging of CB1-receptor expression with [3H]MK-9470**

**Neuro-Pharmacology**

**Neuro-Biology and Personality**

**Metabolism of „Normal Aging“**

**Quantitative Imaging in oncology**

**Preclinical research with small animal PET**

**Quantitative functional parameters derived from PET or conventional scintigraphy to predict efficacy and toxicity of internal radiotherapy**

**Correlation between Opioid-Receptor availability and „Reward Dependence“**

**Apoe4-Polyorphism and metabolic activity**

**Ethanol induced modulation of activation of dopaminergic reward system by opioids**

**4%**

**£ 230,000**

**Cooperation: Department of Psychiatry and Psychotherapy, RWTH Aachen**

**Funding: German Research Foundation Sum.: € 230,000**

**Project Duration: 2011 - 2014**
Department of Radiation Oncology and Radiation Therapy

The Department of Radiation Oncology and Radiotherapy treats approximately 1400 patients with malignant diseases and 150 patients with benign (inflammatory or degenerative) diseases per year. The clinic offers the complete spectrum of tele- and brachytherapy techniques. Special emphasis is placed on multimodality treatment of gastrointestinal malignancies, cancers of the head and neck, brain tumors and sarcoma, precision irradiation of prostate cancer, radiotherapy of malignant lymphomas, breast cancer and other gynecological tumors as well as cranial and extracranial stereotactic irradiation techniques (e.g., radiosurgery of lung tumors). Furthermore, the clinic offers comprehensive expertise for palliative radiotherapy.

The broad spectrum of clinical competence is achieved by sub-specialization of the department's radiation oncologists, extensive internal training and scientific activity. The director of the clinic is a member of a variety of scientific committees and working groups: European guideline for the treatment of germ cell tumors of the testis, Guideline for the treatment of M. Hodgkin, guideline for diagnosis and therapy of gastric carcinoma, Guideline for diagnosis and therapy of esophageal cancer, German Hodgkin lymphoma study group, the German study-group for aggressive non-Hodgkin lymphoma.

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IMPORTANT PUBLICATIONS | MAX.


Clinical research

Malignant lymphomas: HD 1A, HD 17, HD 18: UNFOLDER study in aggressive NHL. Cancers of the head and neck region: pN1 study in cooperation with the Dept. of Oral and Maxillofacial Surgery.

Lung Cancer

Completion of the “PET-Plan” study for the evaluation of PET-based irradiation treatment planning as a basis for dose escalation in the therapy of lung cancer.

Prostate Cancer

PREFERO study (PREFEREnce based randomized evaluation of treatment modalities in low or intermediate risk prostate cancer). The Dept. of Radiooncology and Radiotherapy is the central institution for quality control regarding tele- and brachytherapy in this large multicenter trial.

PASSOS-Study

This retrospective study is aimed at evaluating the radiation dose to the heart during radiotherapy for breast conserving treatment of breast cancer. Patients who have completed their treatment for at least 5 years are analyzed. In cooperation with the Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI) the doses to cardiac substructures are correlated with cardiac events in the later life of the patients. The data of this study will yield new dose constraints for radiotherapy treatment planning.

Brain tumors

Glioblastoma multiforme is the epitome of an aggressive and therapy-resistant tumor entity. A substantial body of evidence suggests that the proliferation of neoplastic astrocytes is strongly dependent upon continuous supply of glucose. Elevated plasma glucose levels, partially as a side effect of anti-epileptic glucocorticoid administration, may, therefore, enhance glioma growth and its therapeutic resistance. In a retrospective analysis led by Dr. A. Mayer, the influence of plasma glucose levels on patient outcome is being investigated.

Translational research

RADIATION: A radiotherapy treatment modality with high local effectiveness but local control of tumor growth can also mitigate the systemic dissemination of tumor cells. Both the tendency for local recurrence and the metastatic potency of carcinomas depend on a diversity of molecular mechanisms of tumor invasion which, therefore, directly influence the outcome of radiation therapy. In turn, these mechanisms are strongly influenced by the tumor microenvironment, which is characterized by a variety of features not observed in healthy, non-cancerous tissue: e.g., hypoxia, acidosis, accumulation of metabolic waste products and elevated interstitial fluid pressure. In a research project led by Dr. A. Mayer, the influence of the tumor microenvironment on therapeutic resistance and mechanisms of tumor invasion is investigated using newly developed research methods for the in situ analysis of patterns of protein expression which allows new insights into pathophysiological interconnections between different cell types. In a second research project, „Biological dosimetry after radiation therapy“ (Dr. Sebastian Zahrener), we are investigating the detection of radiation-induced DNA double-strand breaks in peripheral leukocytes of cancer patients after therapeutic irradiation via assessment of the phosphorylation status of the histone variant H2AX (γ-H2AX) using immunofluorescence methods. This assay is sensitive, suitable for a range of low irradiation doses and can be conducted in a timely manner following radiation exposure. Previously, it was shown that the average number of γ-H2AX foci per peripheral leukocyte immediately after partial body exposure to irradiation exhibits a significant linear dependence upon the integral whole body dose and thus provides a reliable estimate of the applied physical dose. For routine radiotherapy, this opens up an avenue to biodosimetrically compare different radiation techniques in terms of whole-body dose burden to the patient and thus contributes to the best achievable protection of the healthy normal tissues, contributing to a reduced risk for radiation-induced toxicity of normal tissues and secondary malignancies. The project is supported by a Federal Ministry of Education and Research Grant for 3 years (1.703.222 € for the whole project, 259.266 € for the subprojects 2 and 7 which are being conducted in the laboratory of the Dept. of Radiooncology and Radiotherapy in Mainz).
Institutes and Departments of Dental Medicine

- Institute of Dental Materials Science and Technology
- Department of Oral and Maxillofacial Surgery
- Department of Orthodontics and Dentofacial Orthopedics
- Department of Prosthetic Dentistry
- Department of Oral Surgery
- Department of Operative Dentistry
The Institution of Dental Materials Science and Technology divides into two departments: The laboratories of dental preparatory classes on campus and dental treatment facilities as part of Dental-, Oral- and Maxillofacial-clinics at Augustus Square.

Our main task is dental education throughout five terms during preclinical. On campus we have 112 laboratory workstations, including phantom heads at the students’ disposal in order to simulate dental work situations such as the inclusion of crowns, bridges, partial and full dentures.

Dental studies take a most practical approach from the very beginning, whereas dental curriculum has recently been restructured and now focuses on students practically working on phantom heads. This requires cognitive performance as well as fine motor skills and manual dexterity. Scientific emphasis is placed on the evaluation of the teaching; questionnaires are conducted in order to assess the students’ subjective learning progress and wire-bending exercises determine motor skills and their trainability.

Our Dentists perform the entire range of dental treatment. In addition we are specialized in counseling and treatment of patients with intolerant reactions to dental materials such as plastics and alloys.

More and more of the offered courses are supported by multimedia technologies and internet. At present the organization of courses, teaching and testing is primarily based on e-learning at Mainz University. By questionnaires our study in the field of dental propaedeutics evaluated the use and improvement possibilities of Internet-based e-learning as a multimedia tool of learning and teaching processes.

Research activities of the Institute of Dental Materials Science and Technology focus on scientific work referring to intolerance of patients against dental materials such as plastics and alloys. In case of partial dentures, the abutment kinematics and the pressure of the denture base are examined. Using a universal testing facility we determine the bond strength of the metal-ceramic compound and the metal-plastic compound. Contemporaneously the influence of denture adhesives on prosthetic stomatopathy is explored.

Evaluation of cytotoxicity of modified implant-capable titanium-surfaces on human cells
Project Manager: Prof. B Al-Nawas, G Burgard
Project Duration: 2013 - 2015

Evaluation of the practical curriculum in pre-clinical section of the Clinic for Dental, Oral and Maxillofacial Diseases, University Medical Center Mainz
Project Manager: Prof. J Kraft, Dr. V Blaser
Project Duration: 2012 - 2014

In vitro analysis of the internal fit of CAD-CAM milled zirconia bridge frameworks, scanned by the dental scan unit inCOS Blue comparing the CAD-CAM system Sirona InLab MCXL with the milling / grinding unit Datron D5
Project Manager: Prof. H Scheller, S Debatin
Project Duration: 2012 - 2014

Oral health- and oral hygiene situation of Old person and senior citizen’s home inhabitants in the space Mainz
Project Manager: Prof. J Kraft, Dr. J Pistorius
Project Duration: 2012 - 2015

Retrospective study of root resorption after orthodontic treatment on panoramic radiographs
Project Manager: Prof. H Wahrbeck, Dr. A Schamberger
Project Duration: 2011 - 2014
The research focus of the Department of Oral and Maxillofacial Surgery derives from its clinical focus and can be divided into two groups: "tumor biology and reconstructive surgery" and "implantology and bone substitutes", both related to the research field of plastic-reconstructive surgery. Cell culture methods (osteoblasts, fibroblasts, endothelial cells, keratinocytes, cancer cells, endothelial and mesenchymal stem cells) and animal research are used synergistically. There is a close cooperation with departments doing basic research: the former Institute of Applied Structure- and Micromorphology, the Institute of Physiology and Pathopharmacology, the Max Planck Institute for Polymer Research. Biomaterial research is embedded into the University Focus Biomaterials, Tissues and Cells in Science group (BioMatTCS).

Tumor biomidicine

- 10% of the population has oral lesions as risk factors for tumor genesis (oral lichen planus, oral lichenoid lesions, graft-versus-host reaction). Of particular interest is the quality of life of these patients, which is evaluated with special questionnaires in close cooperation with the Department for Hematology, Oncology and Pneumology.

- Oral squamous cell cancer (OSCC) often resists adjuvant therapies through different mechanisms, including upregulation of anti-apoptotic factors and enhanced ROS resistance. The anti-oxidative enzyme PON2 significantly enhances cellular stress resistance and is often upregulated in cancer. Therefore, PON2's still unknown role in protection of OSCC against the repeatedly induced cell death is being investigated. Cellular prognosis parameters influence tumor biology and cancer therapy. The development of new bone substitutes (allogenic bone, xenogenic bone, and local-regional-plastic reconstructions) in addition to masticatory rehabilitation with endosseal implants.

Both operation theatres are equipped for laser and microsurgical surgery. Two cone beam computer tomographies, including the 3D planning software, and two modern ultrasonic machines are used for diagnostics. Furthermore there is an additional cooperation with the Department of Diagnostic and Interventional Radiology of the University Medical Center.

Annualy 1800 operations are performed under local or general anesthesia on 1200 in-patients and an additional 500 out-patients. Approximately 2000 patients are taken care of in special, sometimes interdisciplinary (orthodontics, prosthetics) consultation hours (implantology, tumor, cleft, etc.).

The development of new bone substitute materials (BSM) is of high scientific interest. The aim of this study to evaluate Gtn-HP as a new BSM in oral and maxillofacial surgery.

The development of new bone substitute materials (BSM) is of high scientific and clinical interest in dental surgery as they represent an attractive alternative to autogenous bone grafts. With the vision of establishing injectable hydrogel Gtn-HPa as a new BSM in reconstructive dental surgery, it is the aim of this study to evaluate Gtn-HPa as a matrix for the co-culture of EPC and osteoblasts in 2D and 3D culture. Through these analyses, a hydrogel system with tunable mechanical properties will be examined regarding the interaction of EPC and OB in 2D and 3D culture in order to describe the effects of dimensionality and stiffness of BSM for bone regeneration for the first time and for prospective clinical use.

- Dental, enossous implants are an integral part of the masticatory rehabilitation. In various research groups, materials (titanium alloys, zirconia, PEK) are analyzed in vitro and in vivo studies. The surfaces are analyzed using chemical, mechanical, physical methods. The surface modification with titanium, hydroxyl or proteins is of great interest.

- Allogenic bone substitutes are used for bone reconstruction and augmentation. The influence of these materials on cells is measured with gen and protein expression and SEM. In vivo, these materials are tested in animal and clinical studies.

- Plastic and reconstructive surgery

- The complexity of a masticatory and esthetic rehabilitation after major tissue loss of the head and neck area sometimes requires the use of 3D CAM/CAD methods that are evaluated and developed at our department.

- Deformity and orthognathic surgery are other areas where the long-term success of specific procedures and adjuvant therapies are evaluated.

Important projects and research focus of the Department of Oral and Maxillofacial Surgery.
Department of Orthodontics and Dentofacial Orthopedics

STRUCTURE, FUNCTION AND ORGANISATION OF THE DEPARTMENT

The work of the orthodontic clinic is structured and divided into three main areas. These include the treatment of patients, research in the field of orthodontics and orofacial orthopedics and instruction/training of dental students. The range of treatment covers all orthodontic disorders and abnormalities of children, adolescents and adults. In the Department various removable and fixed appliances are used for treatment. Furthermore aesthetic and invisible treatment is carried out using transparent splint- or fixed lingual appliances. Due to the high percentage of adult patients the Department of Orthodontics and Dentofacial Orthopedics works in close cooperation with the Department of Oral and Maxillofacial Surgery, the Ear, Nose and Throat Department and all additional disciplines in dentistry. A distinct focus of the Clinic is the treatment of orthognathic surgery cases, the use of skeletal anchorage technologies and the treatment and care of patients with cleft lip and palate. The clinics’ facilities have been fully renovated in September of 2009. Since then modern treatment units with all new technical capabilities are available to the physicians and patients.

MAIN FOCUS OF RESEARCH

- Basic research on orthodontic tooth movement cellular reaction of osteoblasts and periodontal fibroblasts under static and mechanical tensile strain
- Cell metabolism during pharmacotherapy and orthodontic force application influence of m-RNA expression of fibroblasts on NISAR in combination with mechanical strain
- Interaction of Orthodontics and Periodontics study on anatomical characteristics and fundamental biological principles for orthodontic tooth movement in the periodontally impaired dentition
- Skeletal anchorage evaluation of different methods for skeletal anchorage (cortical miniscrews and palatal implants) during orthodontic treatment (in cooperation with the Department of Oral and Maxillofacial Surgery, Mainz)
- Caries and Periodontal Prevention during orthodontic treatment studies and evaluation of various materials/products and digital methods to optimize oral hygiene during orthodontic treatment
- Orthodontics after dental and maxillofacial trauma long-term effects after infant dental trauma - retrospective studies on the correction of anklylosed teeth and segments with the use of distraction
- Orthognathic Surgical Treatment long-term stability in dependence of surgical methods and adjuvant treatment modalities
- Cleft lip and palate cleft osteoplasty - extraoral changes in dependence of the transplantsize (3-dimensional studies), orthodontic records and documentation - comparison of different anamnestic questionnaires with the use of the cleft-database, growth and treatment need after early and late palate reconstruction

Fig. 127: GDF-15 protein in periodontal fibroblasts after mechanical strain application (20x)

Fig. 128: Multibracket-appliance treatment in combination with palatal implant anchorage

Fig. 129: Treatment with lingual appliance

Fig. 130: Digital plaque images of the same patient before brushing

Fig. 131: Digital plaque images of the same patient after brushing

IMPORTANT PUBLICATIONS | MAX. 5


IMPORTANT PROJECTS | MAX. 5

Influence of bisphosphonates and mechanical loading on periodontal fibroblasts and osteoblasts
Project Manager: Dr. C Jacobs, Dr. S Grimm, Prof. H Wehrbein
Project Duration: 2011 - 2015

Intraoral Scans in Orthodontics
Project Manager: Dr. S Wriedt, Prof. H Wehrbein
Cooperation: Sinova Dental Systems GmbH
Project Duration: 2010 - 2014

Prevalence of root resorptions after orthodontic therapy with conventional or self-ligating brackets
Project Manager: Dr. C Edie, Prof. H Wehrbein
Project Duration: 2012 - 2015

Study to assess the status of oral health before and in the first 6 months of an orthodontic treatment
Project Manager: Dr. C Edie
Cooperation: Bioscintia GmbH Ingelheim
Funding: University Medical Center Mainz
Sum: € 38,750
Project Duration: 2013 - 2015

The Effect of the Oral-B Triumph Professional Care/TM 9500 Toothbrush in Combination with 0.454% Stannous Fluoride Dentifrice and 0.07% Cetylpyridinium Chloride Mouthrinse on the Reduction of Plaque and Gingival Inflammation in Patients with Fixed Orthodontic Appliances
Project Manager: Dr. C Edie, Prof. H Wehrbein
Funding: Braun GmbH Konberg (Taunus)
Funding: The Procter and Gamble Company Mason Ohio USA
Sum: € 108,000
Project Duration: 2008-2015
The Department of Prosthetic Dentistry is involved in clinical patient care, theoretical and practical education of dental students and clinical and in vitro research.

Within the reach of these work all prosthodontics are covered:
- Fixed partial denture (crowns, bridges)
- Removable partial denture
- Implant supported dentures
- Prosthetic rehabilitation after maxillofacial surgery
- Treatment of cranio mandibular dysfunctions
- Gerostomatology
- Use of CAD/CAM technique
- Aesthetic prosthodontics

To fulfill these tasks, modern methods of diagnostic and therapy are used. The manufacture of dentures can be done in the department’s own laboratory. CAD/CAM technique is used as well as the conventional methods.

Dental students are educated in clinical prosthetic dentistry treating patients by themselves as well as in the student’s dental laboratory. Students are also educated and involved in actual methods of treatment using CAD/CAM technology.

Modern patient treatment assumes clinical and material based research. The department of prosthetic dentistry uses and proves digital technology for diagnostic and planning reasons, for example in 3D-based implantology. Radiological data from a digital volume tomography and model analysis are used to plan the position of dental implants as a “backward planning” before implantation.

Furthermore, clinical studies concerning the long-term survival rate of dentures and the biological compatibility are realised. Another focus in research is the in vitro and in vivo evaluation of ceramic materials. Computer aided methods in manufacturing are applied and examined concerning the precision and clinical outcome. Spectrophotometric colour analysis is utilized and the reproducibility of this method is proved during multiple studies in the department of prosthetic dentistry.

**Important Publications**


**Important Projects**

- An open, prospective, single cohort, multi-centre study evaluating the NobelReplace Conical Connection implants supported single-unit crowns in the maxilla.
  - Project Manager: PD Dr. A Behneke, Prof. N Behneke
  - Funding: Nobel Biocare Services AG, Switzerland
  - Sum: € 35,000
  - Project Duration: 2011 - 2016

- Color variations of three veneering ceramics
  - Project Manager: Dr. M Weyhrauch, PD Dr. K Lehmann, Prof. H Scheller
  - Project Duration: 2012 - 2014

- In vitro analysis of the internal fit of CAD-CAM manufactured Zirkondioxid-framework of fixed partial Dentures using different CAD-CAM-Systems.
  - Project Manager: Prof. H Scheller, S Debatin
  - Project Duration: 2012 - 2014

- Spectrophotometric analyses of surface modifications in a ceramic CAD/CAM material
  - Project Manager: Dr. C Igel, PD Dr. K Lehmann, Dr. V Zinser et al.
  - Project Duration: 2012 - 2014

- The Influence of desinfectant rinseliquids concerning the Interface of dental Implants and Abutments
  - Project Manager: Dr. S Wentaschek
  - Project Duration: 2007 - 2014
The Department of Dental Surgery is responsible for outpatient oral surgery treatment. Examination of new patients in the dental clinic in its entirety is also part of its tasks.

Treatment of patients with severe general diseases and thus increased perioperative risk is a major focus. This includes extended medical diagnosis as well as complex, often interdisciplinary care of patients in cooperation with other departments of the University Medical Center, the Catholic Hospital Mainz, and resident dentists (e.g. screening for infectious foci).

Operations are performed under local anaesthesia or in cooperation with the Department of Anesthesiology (stand-by, sedation, general anaesthesia).

Surgical treatment provides extraction of teeth and osteotomy (destroyed or impacted teeth), tooth preservation operations (root resection, periodontal surgery), laser-surgical soft tissue procedures, augmentation procedures (bone/ soft tissue), tooth traumatology and odontogenic inflammation treatment. Uncovering of impacted or displaced teeth serves to orthodontically move them into their correct position, implants are used as skeletal anchors and for art of rehabilitation.

A key responsibility of the department includes student training on diagnosis and oral surgical treatment of patients as well as techniques of local anaesthesia and dental radiology. In addition, the clinic is in charge of the training of specialists in oral surgery (three-year post-graduate training).

For chronic pain treatment (jaw/ face), diseases of the dental mucous membranes and implantological diagnosis, the clinic offers special consultations. Modern two- or three-dimensional x-ray techniques are available for pre-operative or pre-implantation diagnostics (e.g. Cone Beam CT).

MAIN FOCUS OF RESEARCH

Research Priorities

Acute and chronic orofacial pain

Prof. M. Daubländer, Dr. A. Mourtadidou

Local anaesthesia is of great importance to patients and dentists. Currently, optimization of injection techniques and anaesthesia itself is a major focus of research, besides technical development and improvement (e.g. computer-aided application systems). In-vitro and in-vivo studies on practical application and quality of anaesthesia are also conducted.

Another focus is on patients with cardiovascular diseases that can be triggered by fear, stress and pain as well as by the applied vasoconstrictor (epinephrine) during local anaesthesia. This aims to develop a differentiated approach tailored to the individual needs of such patients.

Diagnosis and therapy of chronic pain using a mechanism-based concept is of increasing importance, especially the differentiation between nociceptive and neuropathic pain. Diagnosis of the underlying mechanisms can be facilitated using psycho-physically examination protocols. Studies with patients suffering from chronic temporo-mandibular dysfunction and neuropathic pain showed relevant results about neuroplastic changes in relation to chronicization and pathogenesis of pain.

Another field of research covers onlay parafunction and sleep disorders in patients with chronic orofacial pain.

Implantology

PD Dr. A. Bohneke, Dr. M. Burwinkel, Dr. K. Knierim

Besides evaluation of clinical long-term approval and testing of therapy concepts of hard- and soft tissue augmentation, new research priorities involve three-dimensional virtual implant planning treatment and static navigation. Minimally invasive surgery is a topic of interest but also testing the accuracy of surgical transmission using different planning and transfer systems. Research activities on implantology are performed in an interdisciplinary context in cooperation with the Department of Prosthetic Dentistry (Prof. N. Behneke).

Another cooperation partner is the Department of Pathology (Dr. S. Ghanati).

Dental Radiology

Prof. R. Schulze, PD Dr. D. Brüllmann, Dr. M. Burwinkel

Prof. R. Schulze works with partners on a project addressing modern three-dimensional radiologic techniques (e.g. cone beam CT/DVT). This project is supported by the Federal Ministry of Education and Research (project: “Lowdoseed*) and carried out by an interdisciplinary working group (dental radiology, mathematics/informatics), initially established by Prof. R. Schulze.

Prof. R. Schulze is also editor of a leading international magazine (Dentomaxillofacial Radiology) and an expert member of various working committees for dental radiology (NADENT at the German Institute for Standardization (DIN)).

Technical procedures using geometric image information, digital image processing and three-dimensional reconstruction from (a few) two-dimensional x-rays are main efforts in this specific field.
Department of Operative Dentistry

Director: Professor Brita Willershausen

University Medical Center Mainz
Augustusplatz 2
D-55131 Mainz
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brita.willershausen@unimedizin-mainz.de
www.unimedizin-mainz.de/zahnreihaltungskunde

Key interests of our duties are the formation and training of dental students and to provide our ambulant patients, based in actual scientific knowledge, with modern dental restorations and materials. The students at the Poliklinik für Zahnreihaltung are compelled to successfully complete three semesters at our facilities in which the they are expected to learn actual theoretical and clinical knowledge of dental pain origin and elimination, root canal treatment, modern resin based materials, gold casting restorations, ceramic inlays as well as with partial crowns. The students are expected to provide our patients with these services under supervision of our clinical and scientific personal. Approximately 5000 out of our 6100 patients are treated solely by students. The three courses offered at our facilities have a capacity for 144 students and are held on a daily basis; occasionally they run parallel.

Further specialties that are offered at the Poliklinik für Zahnreihaltung are Paedodontics (children dentistry) and Periodontology. The final examinations and didactic and patient organization for the next semester are our main activities during the semester holidays.

We have 38 dental units, one of them is dedicated exclusively to root patients with high medical risks and anther for the treatment of children. Our ambulant treatment modalities (approx. 7000 cases a year) are:

- pain emergencies
- traumatia, crown fractures individual and group prophylaxis for children and adults,
- operative dentistry (filings),
- esthetic dentistry, endodontics and
- invasive and non-invasive periodontics.

Flaxural strength. Both are crucial for longevity of dental restorations to avoid marginal gaps as well as cohesive type fractures of the material. In the department or operative dentistry, in vitro shrinkage stress investigations as well as clinical studies on low shrinkage resin composites and on bulk fill restoratives are the main focus of research. The clinical study on a low shrinkage,_slalone-based_material was prolonged to an observation period of a total of four years. A paper as already prepared and will be submitted soon. A clinical split mouth study on the bulk fill restorative Syntac is almost completed and will be published, too. Another focus is on the photopolymerization of resin composite materials: In a clinical survey, more than 500 VLC-devices from more than 300 private dental offices were employed. The results of different root canal preparation systems have been investigated and have shown that none of them is per se capable to completely eliminate the flora from the root canal; thus, the employment of irrigating solutions should be considered as a support to accomplish a complete disinfection of the root canal system.

3. Resin composite restorations, visible light curing, adhesive systems: Resin composites have been continuously developed further on over the last decades. Tremendous efforts had been undertaken to reduce shrinkage stress of those materials and to enhance physical properties as i.e. reduce shrinkage stress of those materials and to enhance physical properties as i.e. 

1. Biocompatibility of dental materials: Endodontic dental materials should fulfil the corresponding requirements. These type of materials are aimed to seal the root canal; thus, a direct contact between them and the periapical tissues can not be avoided. The biocompatibility of these materials, gies such as microscopically, radiologically and by means of micro-tomography. The results of these investigations will be used to develop a precise localization and preparation of the morphological entities of the root canal system. Furthermore, the results of different root canal preparation systems have been investigated and have shown that none of them is per se capable to completely eliminate the flora from the root canal; thus, the employment of irrigating solutions should be considered as a support to accomplish a complete disinfection of the root canal system.

2. Morphology of the root canal system: Accurate knowledge of the root canal system

tem morphology as well as a precise root canal preparation and hermetical filling of the root canal system are decisive factors which play an important role in endodontic therapy success. The morphology of the root foramen and root canal system are dedicated exclusively to root patients with high medical risks and anther for the treatment of children. Our ambulant treatment modalities (approx. 7000 cases a year) are:

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Academic and Research Results


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Central Medical Suppliers

- Pharmacy
- Transfusion Center
Pharmacy

DESCRIPTION OF PHARMACY

The Department of Pharmacy of the University Medical Center Mainz is divided in four activity and organizational sectors, which are:

Pharmaceutical Logistics
This is concerned with the management and supply of medicinal products and medical devices for all patients at the University Medical Center (e.g. drugs, anesthetics, operating theater supplies and implants). Products worth €142 million were supplied in 2013.

Pharmaceutical Production
A special task is the preparation of medicinal products that are not commercially available, that can be produced in-house more cost-effectively and the preparation of products for use in clinical trials. Scope of production in 2013:
- 1,600 extemporaneous preparations in different dosage forms
- 75,000 capsules (of which 52,000 capsules were investigational drugs for clinical trials)
- 124,000 batchwise produced sterile medicinal products
- 30,000 batchwise produced non-sterile medicinal products
- 6,000 total parenteral nutritional solutions for pediatric patients

39,600 ready-to-use cytostatic preparations
147,000 other ready-to-use preparations

Pharmaceutical Services
By the Pharmaceutical Care Services evidence-based, efficient, and cost-effective drug therapy is provided for all patients at the University Medical Center. Key issues are the development of treatment guidelines, drug-use-evaluation, technical reviews, formulary management and controlling the costs of medical products. Ward pharmacists perform a patient individual drug monitoring on specific wards (e.g. intensive care, hemato-oncology) and are responsible for taking the patients’ drug history at admission and counselling discharge medication on other wards (e.g. heart surgery, cardiology). Patients treated with vitamin K antagonists are educated in safe drug usage.

Research
The pharmacy was collaborating in 150 different clinical trials in 2013 (65% sponsored initiated trials, 35% investigator initiated clinical trials). Major tasks are drug preparation, binding, drug account, and documentation.

The aim of the Pharmacy’s research projects is to study the effective and safe use of medicinal products. The results of research are used to optimize the use of medicines and to improve the clinical and social outcomes of drug therapies. For this purpose, we analyze the pharmacological characteristics of ready-to-use drug preparations and investigate the influence of pharmaceutical care and pharmaceutical interventions on the clinical and social outcomes of patients.

Physicochemical compatibility/stability of ready-for-use parenteral preparations
Since many years, the Pharmacy of the University Medical Center has developed a database on the chemical and physical stability of ready-to-use cytostatic preparations. The data documented in the database primarily represent the results of the experimental studies performed in the Pharmacy. In the case of newly approved biologically active substances, physicochemical compatibility of the stock solutions and the ready-to-use injection or infusion solutions is investigated under defined conditions (solid-vent, vehicle solution, storage temperature, exposure to light) by various analytical techniques. The focus of the current studies is the compatibility of biopolymer admixtures containing colistimethate and tobramycin.

Pharmacokinetics
In cooperation with the intensive care unit of the Department of Anesthesiology, the pharmacokinetics of selected antibiotics are studied in critically ill patients suffering from sepsis and acute renal failure demanding for continuous venovenous hemodialysis. HPLC methods were developed to measure the concentrations of piperacillin, ciprofloxacin, meropenem, and linezolid in the serum and dialysate under steady state conditions. The resulting concentration profiles show large inter-individual variations of the resulting serum levels. There is a high risk of underdosage. As a result, the standard dose of piperacillin/tazobactam and ciprofloxacin was already increased.

Effectiveness of pharmaceutical care
Little attention has been paid in Germany to date to the aspects of pharmaceutical care in general and the study of the impact of pharmaceutical care on the clinical, social and economic outcomes of treatment. The impact of ward pharmacists and pharmaceutical care services on the outcome of medication therapy in hospital patients is another topic of our research. The beneficial effects of pharmaceutical care have been demonstrated in several studies. A recent multicenter, open-label study has shown that there are fewer failures to take medication and better patient awareness if pharmaceutical care is provided in the case of discharge medicine. A multi-center study on the influence of single-dose blister packaging on the rate of medication errors was also completed in 2012. Studies of drug compliance in patients prior to organ transplantation and in patients with rheumatoid arthritis are currently being implemented.

SELECTED PUBLICATIONS | MAX. 5


Wolffadt A, Kraemer I, Kamin W. Physicochemical compatibility of nebulizer drug admixtures containing colistimethate and tobramycin. PHARMAZIE. 2013; 68 (9): 744-748.

KEY RESEARCH AREAS

Aerosol characteristics of admixtures of inhalation solutions/suspensions and different nebulizer systems
Project Manager: Prof. I Krämer, PD Dr. W Kahr, H Walf-Jung
Project Duration: 2009 - 2014

Loading, release, stability and compatibility with different contrast media of epirubicin-loaded drug eluting beads
Project Manager: Prof. I Krämer, K Spindler, dr. med.
Project Duration: 2012 - 2015

Medication Compliance and quality of life in patients prior to kidney or liver transplantation, a prospective non-interventional clinical study
Project Manager: Prof. I Krämer, RM Hoeb
Project Duration: 2012 - 2015

Pharmacokinetics of Linolezidine and Meropenem in critically ill patients undergoing enzyme replacement therapy with idursulfase (elaprase®)
Project Manager: Prof. I Krämer, Dr. M Bodenstein, Dr. P Schramm et al.
Project Duration: 2013 - 2015

Screening for neutralizing antibodies and their effects in patients with Morbus Hunter disease (MPS II) undergoing enzyme replacement therapy with idursulfase (Elaprase®)
Project Manager: Prof. I Krämer, Prof. M Beck, M Bayer
Project Duration: 2011 - 2014

Pharmacy

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The Transfusion Center as one of the largest institutions of its kind in Germany, provides all services of current transfusion medicine. This includes blood components, laboratory testing and apheresis-therapy. In addition research deals with aspects of blood donor epidemiology, blood safety, hemovigilance, quality and use of blood components.

1. Blood components supply
The Transfusion Center mainly ensures the supply with blood components. Not only the University Medical Center in Mainz is provided but also surrounding hospitals and regional doctors in practice. A large amount of human plasma for the production of plasma-derivates is also produced. Producing blood products needs continuous enhancement in methods to gain a high level of quality and safety. All methods have to be proven by validation and monitored by a quality assurance system.

2. Transfusion medicine and immunohematologic and transplantation-immunology laboratories
A broad range of methods for immunohematological and transplantation-immunological testing in available to clarify routine and complex diagnostic and clinical aspects. Medical specialists are ready for consultation service in transfusion medicine.

3. Peripheral Blood Progenitor Cell (PBSC) Collection and Apheresis Therapy
Hemapheresis can be an efficient therapy in hematologic and immunologic disorders.

Viral and bacterial risk of transfusion
Regularly new risks for transfusion arise from emerging pathogens or from well known pathogens that become relevant because of epidemic expansion. Research is focused on special aspects in transfusion medicine. Increasing viral and microbial safety of blood components is one of the predominant research focuses. Improving methods for detection of viral nucleic acids has the same importance as generating epidemiologic data for new emerging pathogens, such as West Nile Virus (WNV) and Hepatitis E Virus (HEV). On the basis of the data it is possible to evaluate the residual risk of transfusion-associated infectious complications.

4. Autologous Serum Eye Drops
The Transfusion center is one of few facilities that have a production permit for autologous serum eye drops. The serum-therapy can be the only opportunity to reduce the symptoms of the dry eye. The manufacturing process is carried out in accordance with the European rules of „Good Manufacturing Practice“.

5. Increasing Blood Safety
One of the main challenges in blood supply is the safety of blood components and their application. The Transfusion center has a large laboratory area for processing about 500,000 samples and generating 2,500,000 results per year. Laboratory techniques for screening of blood donors and in-process controls have to be state-of-the-art. New emerging pathogens have to be assessed for potential relevance in hemotherapy.

6. Production of cell preparations for research
Current research in cell therapy and immunology is often based on methods using human white blood cells. The Transfusion center provides leukapheresis products and about 4,000 human white blood cell preparations from whole blood for basic research.

Quality of blood components
The quality of blood components is influenced by the methods of production, handling and storage. Variation of methods affects the quality of plasma significantly. The methods are not standardized worldwide or even in Europe. Investigations about the stability of proteins active in coagulation lead to optimization of freezing and storage of Fresh Frozen Plasma (FFP).

Evaluation and Validation of new methods in immunohematology
Automation of immunohematologic tests is still a diagnostic challenge. The detection of allo-antibodies and blood-group-antigens depends to a great extend on the methods used. Evaluation of new methods affords testing of different patient samples and comparison to molecular based methods such as PCR. Investigations are the basis for regulatory approval of methods.
1. Preliminary Remarks

As a result of the exposure of serious cases of scientific misconduct, the German Research Foundation, the Max Planck Society and the German Rectors’ Conference have drawn up complementary proposals with the aim of preventing the occurrence of such incidents. Rhineland-Palatinate’s Minister for Education, Science and Continuing Education has established a statewide task force that has put together proposals for methods of safeguarding good scientific practice. These proposals represent draft guidelines for the universities in Rhineland-Palatinate.

2. Basic Principles

In medical research, it is expected that the results of research will ultimately take on a concrete form as new diagnostic and therapeutic strategies that will benefit patients. This means that scientists and researchers bear major responsibilities. The welfare and lives of patients often directly or indirectly depend on the results of their work. There are thus consequences arising from such scientific research and the implementation of its results.

- Studies must always be conducted in conformity with the latest scientific information. Awareness of recent publications and appropriate methodology is therefore imperative.
- The methods used and the results must be documented. A fundamental characteristic of scientific research is that it is repeatable, which is only possible if methodologies and results are accurately documented.
- Another fundamental characteristic of scientific research is the aspect of uncertainty. Results of scientific research and their interpretation should continually be assessed until the most plausible explanation for these is identified. This requires, among other things, the proper use of statistical methods.
- Scientific results are communicated in the form of publications. These represent the public announcement of the insight obtained. Thus, they are, like the scientific observation or experience itself, a product of the work of the scientists acting as authors.

3. Recommendations for the Formation of Work Groups

In medicine, several people usually contribute to a specific research project. The individuals who form a work group are thus usually responsible for defining the hypothesis, testing it, interpreting the results, and preparing the report for the scientific community. A responsible approach to research of this type can be facilitated by observing a few simple rules.

- Size of Work Groups

Work groups should not exceed a certain size. A typical work group might have the following composition:

  - A group leader with a postdoctoral lecturing qualification or the equivalent
  - One to three researchers with doctoral degrees
  - One to three doctoral/diploma candidates

The size of groups may vary according to the specific field in which they are working. In larger institutions (e.g., university hospitals), there will usually be several work groups active at any one time.

- Responsibilities of the Director of the Academic Institution

  - The director coordinates the individual work groups and represents the institution externally.
  - The director also implements the overall responsibility that they have for the institution as a whole by delegating responsibility for specific areas to the work group leaders.

- Tasks of the Work Group Leader

  - Definition of the research priorities of the group
  - Specification of work processes and their monitoring
  - Preparation of work programs for doctoral/diploma candidates and guidance with regard to scientific research
  - Organization of weekly laboratory meetings, with laboratory reports by research associates, doctoral and diploma candidates
  - Release of results for publication

- Tasks of Diploma and Doctoral Candidates and Postdoctoral Researchers

  - When they commence their dissertations, diploma and doctoral candidates undertake scientific research. At this time, it is important not only to provide them with the necessary technical skills, but also to ensure that they are familiar with the ethical aspects of research, of the treatment of results and collaboration with other researchers.
  - Through their participation, diploma and doctoral candidates and postdoctoral researchers play a decisive role in determining the research project. They are entitled to regular academic supervision, guidance and support by the group leader. They themselves are required to work responsibly and to collaborate with others.
  - They are required to report regularly on the progress of their research, to participate in internal seminars and, to a limited extent, undertake routine tasks within the work group.
4. Recommendations for Conflict Resolution and Courses of Action in Cases of Suspected Malpractice

The leader of the work group is initially responsible for the resolution of conflicts within the work group. He is obligated to inform his institutional directors about internal conflicts and consult with these when necessary. Should conflicts arise, doctoral candidates should make use of the opportunity to consult with the representative for doctoral candidates of the faculty.

In addition, the Senate of Johannes Gutenberg University has appointed an ombudsman to represent the interests of doctoral and diploma candidates and research associates. The deputy ombudsman works in the field of medicine. If suspicion arises that academic misconduct has occurred (e.g. invention and falsification of data, plagiarism, breach of trust as an expert or supervisor), the guidelines specified above that apply to universities in Rhineland-Palatinate should be followed.

5. Recommendations for Quality Assurance in the Laboratory and Data Documentation

- Quality assurance of studies employing standardized operating procedures must be provided for. It is recommended that quality management systems are put in place at different organizational levels. At the departmental level, the objectives and structure of the department’s quality management system are to be formulated and responsibilities defined.
- If a quality assurance representative for a work group in the laboratory is appointed, the responsibility for implementation of quality management guidelines is delegated to the work group itself. The quality assurance measures for each work group should be summarized in manuals.
- All research projects undertaken by a work group are to be fully documented. These records are legal documents, and are, in accordance to legal regulations, to be archived for at least 10 years.
- Other documents, such as data printouts and films, should be labeled accurately and, for example, filed chronologically. These documents should also be archived for at least 10 years.
- Appropriate measures are to be put in place for the quality assurance of the transfer of data to disks for computerized processing (e.g. duplicate and plausibility checks).
- Electronic data discs with data on which publications are based must be archived in unmodifiable form (e.g., WORM, CD) for at least 10 years.
- Prior to the publication of results, the proposed manuscript must always be submitted to all members of the work group. It is also advisable to present the results to members of other work groups (e.g. at the weekly meetings).
- The methodology employed and findings should be discussed in detail. The authors will benefit because timely criticism of the methodology or interpretation of the findings can be incorporated into the manuscript. The manuscript should be read critically by members of the work group in question and also by other groups (for authorship, see below).
- In the case of projects that involve a statistical analysis of research results, it is advisable prior to commencement to consult with the Institute of Biomedical Statistics and Documentation or a similar institution regarding the proposed experimental design and statistical procedures to be used.

6. Authorship of Scientific Publications

Design of Scientific Publications

- Original publications are used to communicate new observations or experimental results, including conclusions. Hence the repeated publication of the same results is not a permissible practice.
- Scientific research must be verifiable. Hence publications must contain an accurate description of the methodology employed and the results obtained.

Criteria for Authorship of Scientific Publications

To be considered the author of a research report of a work group and thus also responsible for the report, a researcher must have contributed significantly

1) to the project in the form of participation in the formulation of the research hypothesis, formulation of the research plan, evaluation of results, interpretation of results and the drafting or critical review of the manuscript.

Both requirements must be met. Those who provide financial support to the project, manage the institution in which the research was conducted or read the manuscript are not entitled to be considered authors.

With regard to the ethical aspects of research projects of the department or work group, institutional directors and subordinate research associates are subject to the instructions and recommendations of the local ethics committee and the animal protection committee. In addition, researchers are to ensure that to the best of their knowledge and belief, they are able to comply with the relevant laws and regulations of the competent authorities and institutions.

In reports that are authored by several work groups, the contribution of each group should be identified.

A form permitting the release of a manuscript for publication should be signed by all authors and the contributions of individual authors are to be identified (see form in the appendix).

If unpublished observations of other persons are cited in the manuscript, findings of other institutions are used, or other persons thanked, their written consent must be obtained.

Diploma and doctoral candidates whose results are included in the publication are to be cited as co-authors. If these have not yet completed their diploma/dissertation, it should be noted in the acknowledgment that the publication contains data from the dissertation of the person(s) concerned.
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