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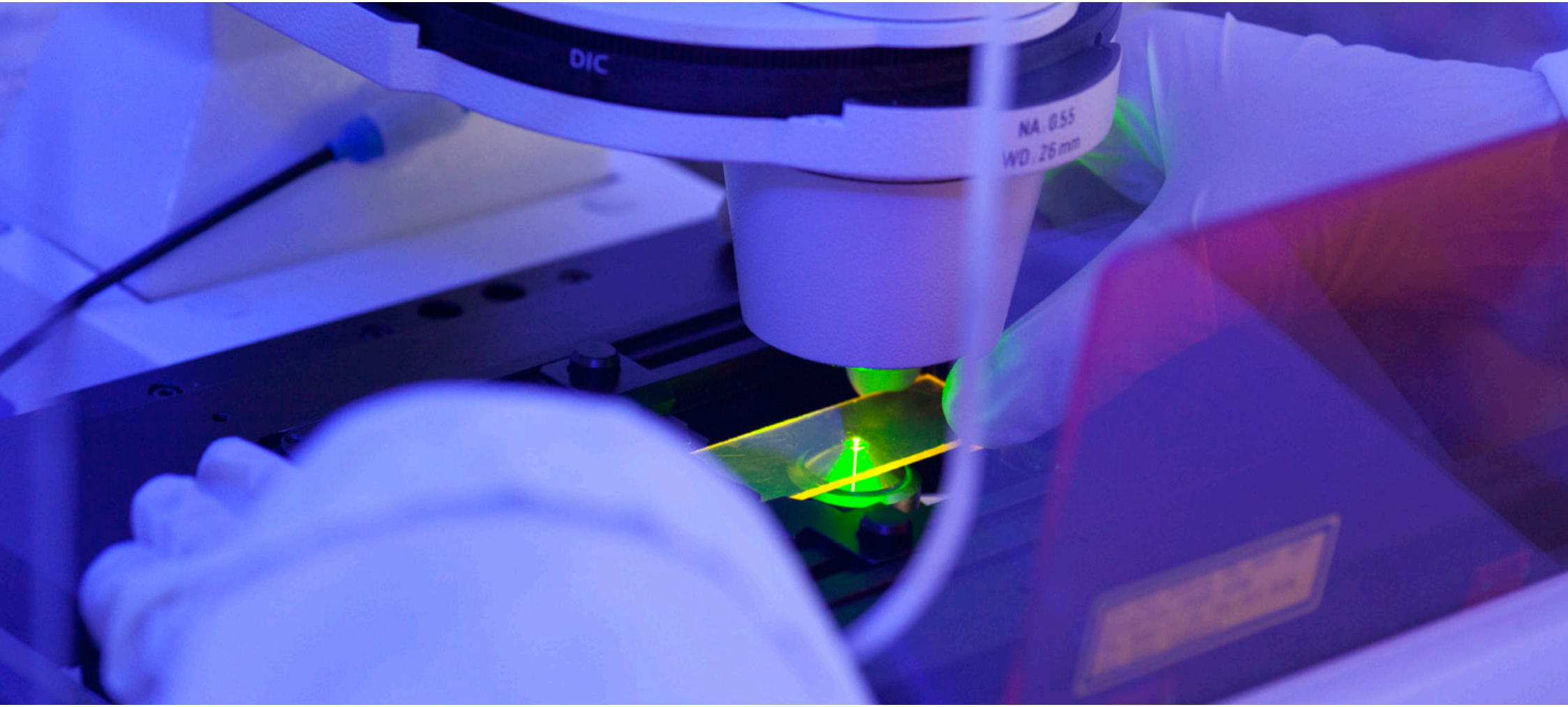

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Welcome Address

It is our great pleasure to present this edition of “Ulm University Medicine – Research & Teaching 2015”. You will find details of all the latest developments and newest achievements of the Medical Faculty Ulm and of the Ulm University Medical Center.

Ulm University Medicine is dedicated to providing excellent teaching and training for our future scientists and physicians in order to enhance high quality research and health care. Since the publication of our last report in 2010, the Medical Faculty and Ulm University Medical Center have progressed tremendously. Recent endeavours amongst others include the Collaborative Research Center 1074 – “Experimental Models and Clinical Translation in Leukemia” (Speaker: Prof. Hartmut Döhner), the Collaborative Research Center 1149 – “Danger Response, Disturbance Factors and Regenerative Potential after Acute Trauma” (Speaker: Prof. Florian Gebhard), both funded by the German Research Foundation (*Deutsche Forschungsgemeinschaft, DFG*), and our Comprehensive Cancer Center Ulm - CCCU (Speaker: Prof. Hartmut Döhner), which was positively evaluated in 2014 and is funded by German Cancer Aid (*Deutsche Krebshilfe*) as a Center of Excellence in oncology. Based on a comprehensive approach to health care, this center is committed to combining high level basic and translational research, high quality teaching of students and the training of junior scientists and clinicians with state-of-the-art medical care for the benefit of our tumor patients.

We have obtained several grants for novel collaborative research projects that are funded, for instance, by the German Federal Ministry of Education and Research (BMBF) and the EU. These projects deal with a variety of fields among which are: Molecular Systems Biology of Impaired Stem Cell Function and Regeneration during Aging – SyStaR (Speakers: Prof. Karin Scharffetter-Kochanek, Prof. Hans Kestler, Prof. Hartmut Geiger), Mental Healthcare for Children and Adolescents after Abuse and Neglect (Speaker: Prof. Jörg Fegert), and Medical and Psychosocial Implications of Extreme Obesity in Adolescents (Speaker: Prof. Martin Wabitsch). We are especially proud that our colleague Prof. Frank Kirchhoff has received an Advanced Grant of the European Research Council (ERC) for his research project entitled “The AntiVirome: A Combined Evolutionary and Proteomics Approach to the Discovery, Induction and Application of Antiviral Immunity Factors”. And last but not least, our International Graduate School in Molecular Medicine Ulm – IGradU (Chairman: Prof. Michael Kühl) was positively reevaluated in 2012 and will continue to be funded by the Excellence Initiative of the German federal and state governments until 2017. At this Graduate School nearly 200 PhD students from all over the world are trained according to the highest international standards. Under the roof of IGradU, a new DFG-funded Research Training Group (GRK 1789) has recently been established entitled CEMMA: Cellular and Molecular Mechanisms of Aging (Speaker: Prof. Hartmut Geiger).

To improve the research infrastructure, Ulm University Medicine has launched an innovative core facility concept. Core units already operating include our genome center (deep-sequencing, chip analyses and a bioinformatics facility), a proteomics unit, confocal and multiphoton microscopy, a transgenic mouse facility, small animal imaging, a cell sorting facility, and a 3 Tesla Whole-Body MRI.

To transfer new scientific insights quickly from lab to bench scientists and clinicians work closely together. Their expertise is complemented by state-of-the art equipment and technology. Just a few examples: Our new Center of Surgery, located in the immediate vicinity of a wide range of other departments and Ulm Science Park, enhances our multidisciplinary approach to excellence in patient care. Within the Comprehensive Cancer Center Ulm our clinicians and scientists develop innovative treatment of patients suffering from leukemia and lymphoma. Our new multidisciplinary Imaging Center delivers high end diagnosis. The recently founded Center for Rare Diseases (Speaker: Prof. Frank Lehmann-Horn) works as part of a nationwide network. Our aim is to constantly improve diagnostic and treatment options for the benefit of our patients.

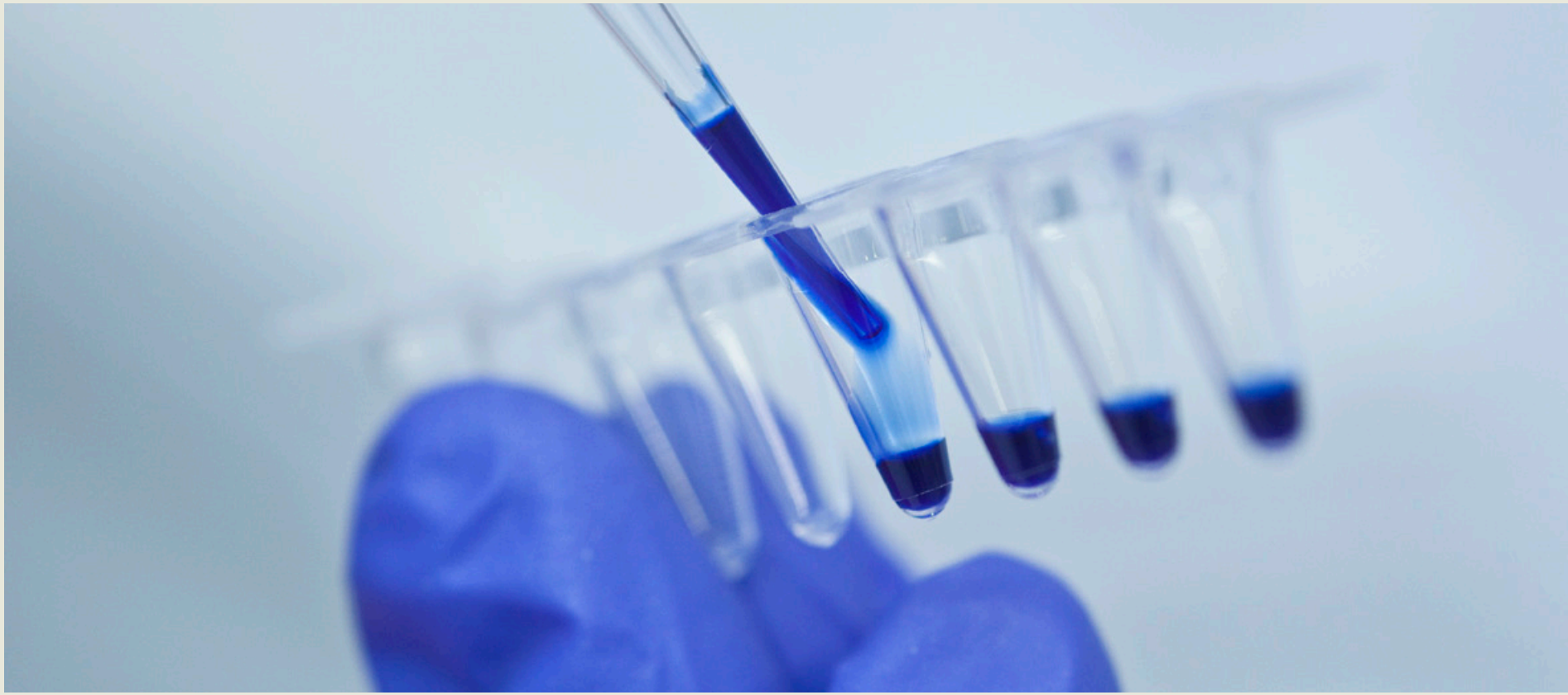


What are our future plans and visions? We are committed to expanding our standing and reputation within the national and international scientific community. On the one hand, this will entail the further development of our research infrastructure in order to establish such new core facilities as a unit for animal phenotyping. On the other hand, our high level teaching and training programs will be expanded for the increasing numbers of talented students entering the fields of human medicine, dentistry and molecular medicine. This plan includes the introduction of a new master course of studies in Molecular and Translational Neuroscience together with the Faculty of Natural Sciences as well as double degrees at Master and PhD levels in collaboration with our partner universities in Oulu, Finland and Padua, Italy.

Finally, we would like to thank all those institutions, both national and international, which have been and still are involved in making Ulm University Medicine the great success that it has become. Their enthusiasm has given us ample motivation to further our efforts and continue fulfilling our mission to strengthen both the quality of and innovations in medical research and teaching.

Prof. Dr. Thomas Wirth
Dean Medical Faculty

Prof. Dr. Klaus-Michael Debatin
Medical Director Ulm University Medical Center



Scientific Profile

The best universities worldwide at the age under 50 years (Source: timeshighereducation.co.uk)

1	Pohang University of Science and Technology	Republic of Korea	69.8
2	École Polytechnique Fédérale de Lausanne	Switzerland	68.3
3	Korea Advanced Institute of Science and Technology	Republic of Korea	67.4
4	Hong Kong University of Science and Technology	Hong Kong	65.3
5	Nanyang Technological University	Singapore	61.7
6	Maastricht University	Netherlands	60.4
7	University of California, Irvine	United States	59.3
8	Université Paris-Sud	France	56.2
9	Université Pierre et Marie Curie	France	56.1
10	Lancaster University	United Kingdom	55.4
11	University of California, Santa Cruz	United States	54.4
12	University of Warwick	United Kingdom	54.0
13	University of Illinois at Chicago	United States	51.2
13	Pompeu Fabra University - Barcelona	Spain	51.2
15	The University of Texas at Dallas	United States	50.6
16	Universität Ulm	Germany	49.9
17	City University of Hong Kong	Hong Kong	49.0
17	Université Paris Diderot - Paris 7	France	49.0
19	University of Calgary	Canada	47.6
20	Universität Konstanz	Germany	47.3
21	University of Milan-Bicocca	Italy	47.0
22	University of Essex	United Kingdom	45.5
23	Autonomous University of Barcelona	Spain	44.9
24	Simon Fraser University	Canada	44.6
24	Swedish University of Agricultural Sciences	Sweden	44.6
26	Université Montpellier 2	France	44.5
27	Sharif University of Technology	Iran	44.1
28	The University of Newcastle	Australia	43.6
29	Brunel University London	United Kingdom	43.4
30	Hong Kong Polytechnic University	Hong Kong	43.2
31	Bilkent University	Turkey	42.9
31	Queensland University of Technology	Australia	42.9
33	University of Wollongong	Australia	42.6
34	University of Bath	United Kingdom	41.6
34	Macquarie University	Australia	41.6
36	Medical University of Vienna	Austria	41.5
37	University of Southern Denmark	Denmark	41.1
37	State University of Campinas	Brazil	41.1
39	Umeå University	Sweden	40.5
40	National Sun Yat-Sen University	Taiwan	40.4
41	Koç University	Turkey	40.1
42	Plymouth University	United Kingdom	40.0
42	National Taiwan University of Science and Technology	Taiwan	40.0
44	University of Waikato	New Zealand	39.5
44	University of Tsukuba	Japan	39.5
46	Linköping University	Sweden	39.4
47	University of Technology, Sydney	Australia	39.2
48	University of Crete	Greece	38.6
49	University of South Australia	Australia	38.4
49	Universität Bayreuth	Germany	38.4

The *Times Higher Education 100 Under 50 2014* is a ranking of the top 100 universities under 50 years old. (Rankings 51 to 100 can be viewed at timeshighereducation.co.uk/world-university-rankings/2014/one-hundred-under-fifty.) It provides a glimpse into the future, showcasing not those institutions with centuries of history, but the rising stars which show great potential. The table employs the same 13 separate indicators as the Times Higher Education World University Rankings, but the 100 Under 50 2014 methodology has been carefully re-calibrated to reflect the special characteristics of younger universities, giving less weight to subjective indicators of academic reputation.

Scientific Profile

Ulm University Medicine (*Universitätsmedizin Ulm*) is one of the top performing medical institutions in the fields of biomedical and clinical research in Germany. In the recently published Times Higher Education Ranking 2014 of "The 100 under 50", which ranks the top 100 universities under 50 years, Ulm was ranked in sixteenth position worldwide. As a consequence, Ulm University represents the best of the newest universities in Germany. Ulm University was particularly outstanding under the criteria of "citations in scientific journals" and "international orientation." Among the most cited articles, medical research is predominant, with oncology receiving more citations than any other research field at Ulm University and the neurosciences being ranked in third place. The international orientation of Ulm University is positively influenced by the International Graduate School in Molecular Medicine Ulm (see page 56, 62 and 82).

The Research Profile of Ulm University Medicine covers the following areas:

- **Molecular Mechanisms of Aging and Age-associated Diseases**
  - **Aging, Stem Cell Aging, Signal Transduction Pathways, Apoptosis**
  - **Hemato-Oncology**
  - **Rare Neurodegenerative Diseases**
  - **Cardiometabolic Diseases (Diabetes and Obesity)**
- **Trauma Research (physical and psychic)/Musculoskeletal Research**
- **Cross-sectional Centers**
- **Additional Topics**

External third-party funding of research totaled approximately €50.9 million in 2013 and included grants for collaborative research networks of the German Research Foundation (DFG), the Excellence Initiative of the German federal and state governments (*Exzellenzinitiative des Bundes und der Länder)*, the German Federal Ministry of Education and Research (BMBF), the European Union, the State of Baden-Württemberg and the Helmholtz Association in addition to such foundations as German Cancer Aid (*Deutsche Krebshilfe*), the *Else Kröner-Fresenius-Stiftung* and the CHDI Foundation (a privately funded and not-for-profit biomedical research organization devoted to Huntington's disease based in the USA). The topics of these research networks are described in detail from page 25 onwards. They are grouped under common headings into scientific centers which act as nuclei for novel research networks.

These centers include the Center of Cellular Decision and Signaling Pathways during Aging, the Center of Emergency Response and Regeneration after Musculoskeletal Trauma, the Center of Rare Diseases, and the Center of Child Protection in Medicine in Baden-Württemberg (run in conjunction with the medical faculties of Heidelberg and Mannheim).

Enhancing our Research Profile by promoting dialogue and cooperation



In 2009, the Center of Medicine and Society was founded with the mission to promote dialogue between future-oriented research in the field of biomedical sciences and society within the context of the basic historical, theoretical and ethical principles of medical research and action. The program entitled "Join the Healthy Boat" („Komm mit in das gesunde Boot") is a program for health promotion that encourages the healthy development of children in primary schools and schools with learning support by focusing on physical activity, nutrition and recreational activities. All these centers are financially supported by the State of Baden-Württemberg.

In 2011, an agreement of cooperation was signed with the Public and Private Partnership Research Association BIU (Boehringer Ingelheim Ulm University BioCenter). This research association focuses on neurodegenerative, cardiometabolic and lung diseases. The BioCenter is supported by Boehringer Ingelheim, the State of Baden-Württemberg and the Medical Faculty of Ulm University.

The Comprehensive Cancer Center Ulm (CCCU), which is supported by a grant from German Cancer Aid, was established in 2007 with the goal of combining state-of-the-art clinical research with clinical care and the education and training of junior researchers and clinicians for the direct benefit of tumor patients.

Research in the field of neurosciences has been strengthened by the interdisciplinary Neuroscience Center Ulm operated by the faculties of Medicine, the Natural Sciences as well as Engineering and Computer Science. Research topics at this center range from molecular basics to neurological and psychiatric syndromes based on the concept of "from gene to behavior." The Transfer Center of Neurosciences and Learning (*Transferzentrum für Neurowissenschaften und Lernen, ZNL*) was established in 2004 with the financial support of the State Foundation of Baden-Württemberg (*Landesstiftung Baden-Württemberg*) and the Free State of Bavaria (*Freistaat Bayern*) with the aim



Life Science Building, Ulm University

of implementing the neuroscientific findings of basic research into teaching practice in order to improve both teaching methods and learning performance. The ZNL employs an interdisciplinary approach by means of a team that comprises psychologists, physicians and educationalists.

One of the most important tasks of the Medical Faculty and Ulm University Medical Center is to provide a comprehensive infrastructure and supportive environment to assist scientists and junior researchers to focus on their projects. For instance, our program *Gerok Positions* offers young clinicians the possibility of concentrating on their research for a period of one to two years during which they are free of any clinical obligations. Similarly, the Hertha-Nathorff Program supports junior female physicians of outstanding talent to develop their scientific career through rotation positions for up to one year. Several graduate and postgraduate programs have also been introduced to support PhD students and postdocs. These programs, which are described in detail on page 66, start with attractive fellowships and lead to financial support for subsequent research projects.

The research infrastructure includes modern laboratories such as our Life Science Building inaugurated in 2008.

Enhancing our Research Profile by improving the infrastructure

A complementary innovation for strengthening scientific performance is the implementation of core facilities at the Medical Faculty of Ulm University that provide resources for shared cross-institutional use and for external partners. These core facilities are specifically:

- Confocal and Multiphoton Microscopy Facility
- FACS (Fluorescence Activated Cell Sorting) Facility
- Genomics Facility
- Core Unit Mass Spectrometry and Proteomics
- Small Animal Imaging Facility
- Transgenic Mice Facility
- 3 Tesla MR Imaging in Human Neuroscience

(please see page 15 onwards)

The development of additional facilities is ongoing, such as the extension of our Bioinformatics Facility into a Department of Bioinformatics and Systems Biology, in order to respond to rapid developments in the field of biomedical research.

Enhancing our Research Profile by targeting appointments

Over the last few years a specific research profile of the Medical Faculty of Ulm University was established and enhanced by selective appointments. These are in particular:

- Prof. Dr. rer. nat. Gilbert Weidinger, Institute of Biochemistry and Molecular Biology, 2012
- Prof. Dr. med. Thomas Seufferlein, Department of Internal Medicine I, 2012
- Prof. Dr. med. Christian Beltinger, Department of Pediatrics and Adolescent Medicine, 2012
- Prof. Dr. med. Wolfgang Janni, Department of Gynecology and Obstetrics, 2012
- Prof. Dr. med. Thomas Hoffmann, Department of Otorhinolaryngology, 2013
- Jun-Prof. Dr. rer. nat. Steffen Just, Department of Internal Medicine II, 2013
- Prof. Dr. med. Manuela Dudeck, Department of Forensic Psychiatry and Psychotherapy, 2013
- Prof. Dr. rer. nat. Stefan Reber, Department of Psychosomatic Medicine and Psychotherapy, 2013
- Prof. Dr. med. Jens Huober, Department of Gynecology and Obstetrics, 2013
- Prof. Dr. med. Nicolas Rüsch, Department of Psychiatry and Psychotherapy II, 2013
- Prof. Dr. med. Hasan Jumaa, Institute of Immunology, 2013
- Prof. Dr. med. Anne-Karoline Ebert, Department of Urology, 2013
- Prof. Dr. med. Meinrad Beer, Department of Diagnostic and Interventional Radiology, 2013
- Prof. Dr. med. Oliver Zolk, Institute of Naturopathic Medicine and Clinical Pharmacology, 2013
- Prof. Dr. phil. Lutz Goldbeck, Department of Child and Adolescent Psychiatry/Psychotherapy, 2014
- Prof. Dr. med. Ambros Beer, Department of Nuclear Medicine, 2014
- Jun-Prof. Dr. rer. nat. Jens von Einem, Institute of Virology, 2014
- Prof. Dr. rer. nat. Manfred Frick, Institute of General Physiology, 2014
- Jun-Prof. Dr. biol. hum. Daniel Sauter, Institute of Molecular Virology, 2014
- Prof. Dr. phil. Georg Grön, Department of Psychiatry and Psychotherapy III, 2014
- Prof. Dr. med. Guntram Borck, Institute of Human Genetics, 2014
- Prof. Dr. med. Alexander Meining, Department of Internal Medicine I, 2014





Prof. Dr. Klaus-Michael Debatin, Head of the Department of Pediatrics and Adolescent Medicine, Ulm University (right) was honored with the German Cancer Aid Award in 2011 by Dr. h.c. Fritz Pleitgen, President of German Cancer Aid (left).



The Innovation Prize of the German Society for Trauma Surgery (DGU) was awarded in 2012 to Prof. Dr. Anita Ignatius, Head of the Institute of Orthopedic Research and Biomechanics, Ulm University (right), and Prof. Dr. Markus Huber-Lang of the Department of Orthopedic Trauma, Hand, Plastic and Reconstruction Surgery, Ulm University (left).

Prestigious Awards

How can we rate the success of all of these initiatives? Third-party funding, the extensive publication of papers, and the many awards received all bear witness to the extent of this success. As described above, scientists of the Medical Faculty and the University Medical Center Ulm receive more than 50 million euros in third-party funds each year and this is steadily increasing. In 2013, they published 1,168 papers and have been honored with a growing number of recognized awards, for example, the German Cancer Aid Award (2011, Prof. Dr. Klaus-Michael Debatin), the DGU Innovation Prize (2012, Prof. Dr. Anita Ignatius, Prof. Dr. Markus Huber-Lang), the Ernst Schering Prize (2013, Prof. Dr. Frank Kirchhoff), the SIU Distinguished Career Award (2013, Prof. em. Dr. Dr. h.c. Richard Hautmann), the Rudolf Schönheimer Medal (2014, Prof. Dr. Wolfgang König), the Pritzker Prize of the Michael J. Fox Foundation (2014, Prof. Dr. Heiko Braak) and the José Carreras Award (2014, Prof. Dr. Hartmut Döhner), to name but a few.



Prof. em. Dr. Dr. h.c. Richard Hautmann, former Head of the Department of Urology, Ulm University, received the SIU (Société Internationale d'Urologie) Distinguished Career Award in 2013.



The Rudolf Schönheimer Medal was awarded to Prof. Dr. Wolfgang König, Department of Internal Medicine II, Ulm University, in 2014.



The Ernst Schering Prize was awarded to Prof. Dr. Frank Kirchhoff, Head of the Institute of Molecular Virology, Ulm University, in 2013.

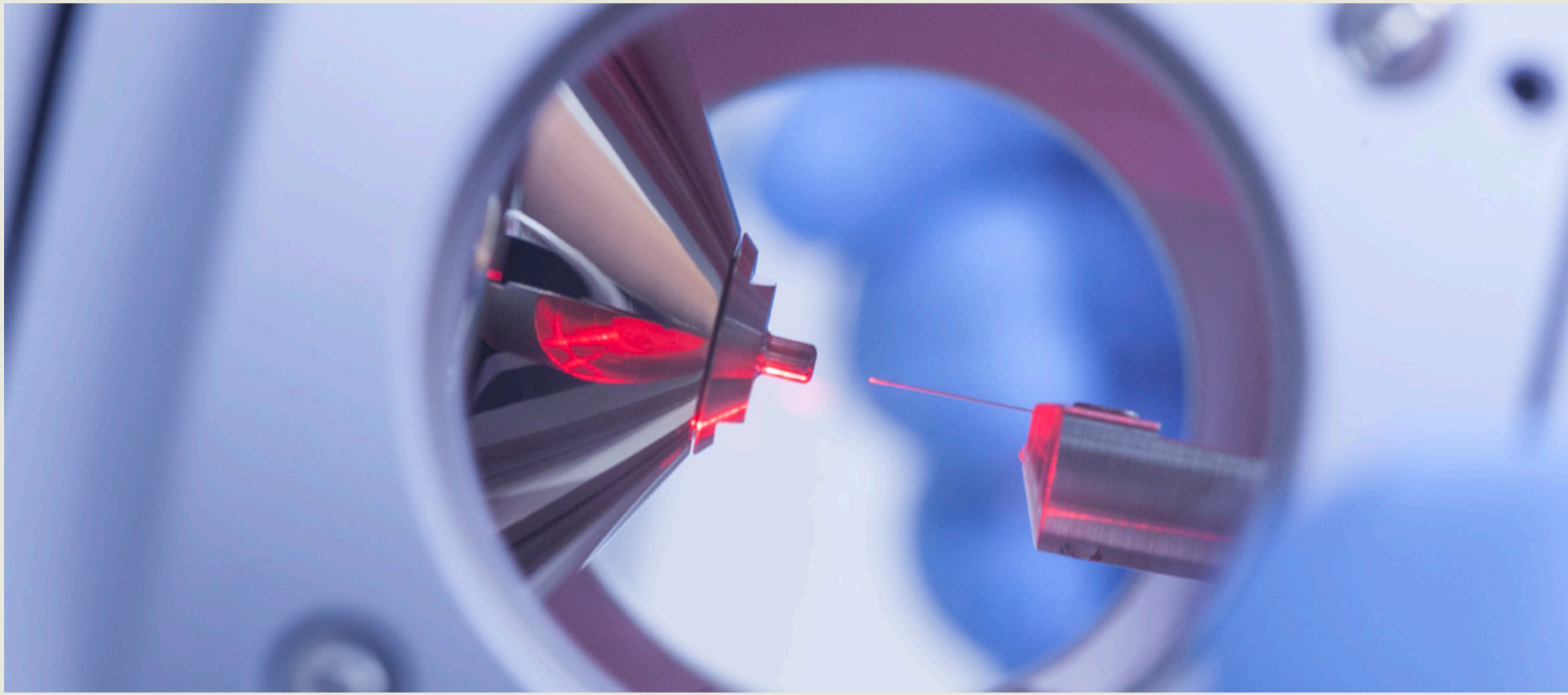
We are extremely proud of these achievements. However, according to the motto “to stand still is a step backwards,” we are always striving to improve our infrastructure and to recruit the best scientists for our institutes and departments with the aim of strengthening not only our scientific profile but also our firm position in the national and international scientific community. For instance, novel collaborative research networks have been initiated to cover such topics as leukemias and lymphomas, stem cell biology, aging, cardiometabolic and rare neurodegenerative diseases to mention the most advanced initiatives being undertaken. In addition, we established a transdisciplinary Trauma Research Center to focus on the close connection between physical and psychological trauma so that the results of basic research can be transferred to medical practice as soon as possible for the benefit of our patients. The last two points, in particular, are a major challenge and will be a guiding factor in the future development of the *Universitätsmedizin Ulm*.



Prof. Dr. Hartmut Döhner, Head of the Department of Internal Medicine III, Ulm University (right), received the José Carreras Award of 2014 from the European Hematology Association, EHA.



The awarding of the Robert A. Pritzker Prize in 2014 from the Michael J. Fox Foundation to Prof. Dr. Heiko Braak, Senior Professor at the Department of Neurology, Ulm University (left) by Michael J. Fox (right) and Dr. Todd Scherer, CEO of the Michael J. Fox Foundation (middle).



Research Infrastructure

A complementary innovation for strengthening scientific performance is the implementation of core facilities at the Medical Faculty of Ulm University that provide resources for shared cross-institutional use and for external partners.

These core facilities are specifically:

- Confocal and Multiphoton Microscopy Facility
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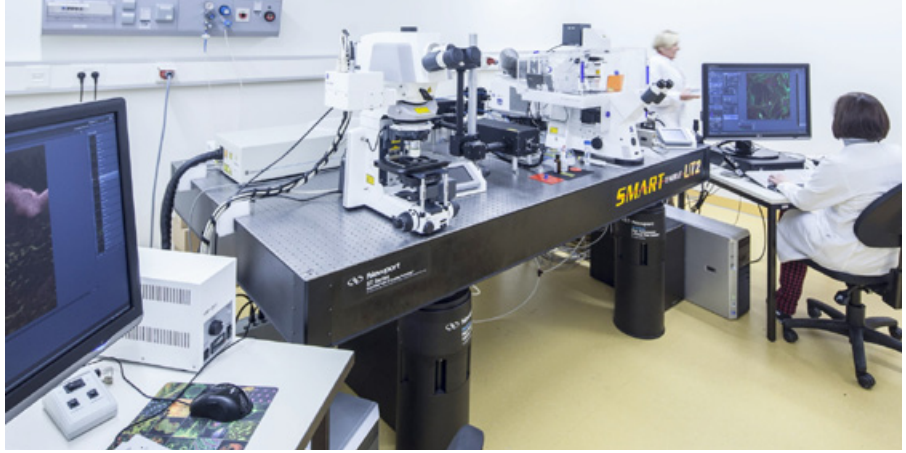
- Core Unit Mass Spectrometry and Proteomics
- Small Animal Imaging Facility
- Transgenic Mice Facility
- 3 Tesla MR Imaging in Human Neuroscience



The heart of the core unit:
LSM 710 (right); LSM 7 MP (left);
and fs-pulsed Ti:Sa laser (middle).

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Medical Faculty
Core Facility Confocal and Multiphoton Microscopy
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http://fakultaet.medizin.uni-ulm.de/forschung/core-facilities/lasermikroskopie/

Core Facility

Confocal and Multiphoton Microscopy

Head of Core Facility: Dr. Angelika Rueck

Keywords: Functional confocal imaging | multiphoton | FLIM | FRET | SHG

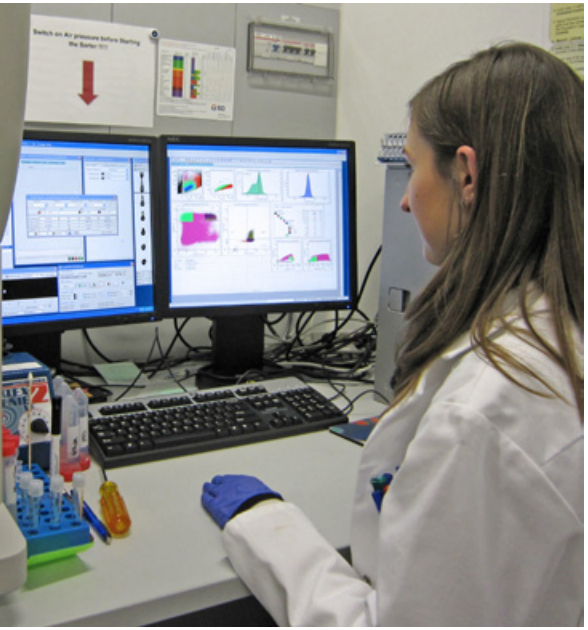
The core unit “Confocal and Multiphoton Microscopy” is located in the Medical Faculty of Ulm University. The heart of the unit consists of two laser scanning microscopes, one being an inverted LSM 710 and the other an upright microscope LSM 7 MP. Both microscopes are coupled to an fs-pulsed laser to provide multiphoton microscopy. Besides spectral detection and time-resolved detection, detailed fluorescence lifetime imaging (FLIM) is now possible with the newest generation of hybrid detectors and TCSPC electronics. In addition to the LSM 710, the LSM 510 META is equipped with a spectrometer for spectral imaging which is utilized at the facility. There are also labs available for cell culturing and molecular biology.

The core unit “Confocal and Multiphoton Microscopy” has existed in its current form since August 2013. It functions as a life cell imaging competence center, mainly for the purposes of biomedical research. At present there are seven people (five females and two males) working at the facility. Two of them (the head and the first assistant) have permanent positions while the others hold temporary positions in research projects. The aim of these projects is the development and adaption of new imaging techniques, for example phosphorescence lifetime imaging, that can be helpful for other users. Fees are requested for the use of this core unit.

Some of the highlights of our scientific topics include cell-cell adhesion, protein interaction, transport processes, cell metabolism, nanoparticles, stem cell research, wound-healing, sepsis and developmental biology.

Selected Publications:

- *Rueck A, Hauser C, Lorenz S, Mosch S, Rotte S, Kessler M, Kalinina S (2013): Cell metabolism, tumour diagnosis and multispectral FLIM. Proc. SPIE DOI: 10.1117/12.2003729 (2013).*
- *Amin RM, Hauser C, Kinzler I, Scalfi-Happ C, Rueck A (2012): Evaluation of photodynamic treatment using Aluminum PhthalocyanineTetrasulfonate Chloride as a photosensitizer: New approach. Photochem. Photobiol. Sci., ID PP-ART-12-2011-005411.R1.*
- *Rueck A, Lorenz S, Hauser C, Mosch S, Kalinina S (2012): Multiwavelength FLIM: New concepts for fluorescence diagnosis. Proc. SPIE DOI: 10.1117/12. 906620.*
- *Florian MC, Dörr K, Niebel A, Daria D, Schrezenmeier H, Rojewski M, Filippi M-D, Hasenberg A, Gunzer M, Scharffetter-Kochanek K, Zheng Y, Geiger H (2012): Cdc42 Activity Regulates Hematopoietic Stem Cell Aging and Rejuvenation. Cell Stem Cell, 10 (5): 520 – 530.*
- *Strat D, Dolp F, von Einem B, Steinmetz C, von Arnim CAF and Rueck A (2011): Spectrally resolved fluorescence lifetime imaging: FRET Global Analysis with a one- and two-exponential donor model. Journal of Biomedical Optics, 16(2), 026002.*



Isolation of murine hematopoetic stem cells via complex multicolor FACS (Fluorescence Activated Cell Sorting) on a BDFACSAriaIII cell-sorting machine.

Core Facility

FACS – Fluorescence Activated Cell Sorting

Head of Core Facility: Prof. Dr. Christian Buske
Coordinator FACS: Prof. Dr. Christian Buske
Keywords: Fluorescence activated cell sorting | FACS

The newly established core facility of Fluorescence Activated Cell Sorting (CF-FACS) is part of the Medical Faculty of Ulm University. The facility is fully run by a coordinator and FACS operator and offers an advisory and complete sorting service for its users with the support of three FACS operators.

The CF-FACS is equipped with the following machines from the company Becton Dickinson: Sorter 1: FACS Aria 3 fitted with five lasers (375, 405, 488, 561 and 633 nm); Sorter 2: FACS Aria 3 fitted with four lasers (375, 405, 488 and 633 nm); Sorter 3: FACS Aria 2u fitted with three lasers (405, 488 and 633 nm); and Sorter 4: BD LSR II with four lasers (325, 405, 488 and 633 nm). Different filter combinations are available that enable the measurement of almost all fluorochromes available on the market. We own ceramic duct nozzles of different sizes (70, 85 and 100 um) that allow the sorting of cells of various diameters up to 25 µm. On all machines it is possible to sort up to four different cell populations out of one probe into 1ml, 5ml and 15ml tubes, as well as multi- or single-cell sorting into multi-well culture plates. Sorters 1 and 2 are additionally equipped with an aerosol vacuum device that enables sorting of infectious organisms and gene-modified cells classified as biosafety S2.

A large number of institutes of Ulm University and the University Hospital Ulm benefited from the service of the CF-FACS in the year 2013. The main focus of the research projects that run on the machines of the CF-FACS has centered on stem cell biology, cancer and aging.

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http://fakultaet.medizin.uni-ulm.de/forschung/core-facilities/facs/

Selected Publications:

- *Edmaier KE, Stahnke K, Vegi N, Mulaw M, Ihme S, Scheffold A, Rudolph KL, Buske C (2014): Expression of the lymphoid enhancer factor 1 is required for normal hematopoietic stem and progenitor cell function. Leukemia, 28(1):227-30.*
- *Zhou X, Florian MC, Arumugam P, Chen X, Cancelas JA, Lang R, Malik P, Geiger H, Zheng Y (2013): RhoA GTPase controls cytokinesis and programmed necrosis of hematopoietic progenitors. J Exp Med., 210 (11): 2371-85.*
- *Luche H, Nageswara Rao T, Kumar S, Tasdogan A, Beckel F, Blum C, Martins VC, Rodewald HR, Fehling HJ (2013): In vivo fate mapping identifies pre-TCRα expression as an intra- and extrathymic, but not prethymic, marker of T lymphopoiesis. J Exp Med., 210(4):699-714.*
- *Florian MC, Nattamai KJ, Dorr K, Marka G, Uberle B, Vas V, Eckl C, Andra I, Schiemann M, Oostendorp RA, Scharffetter-Kochanek K, Kestler HA, Zheng Y, Geiger H (2013): A canonical to non-canonical Wnt signalling switch in haematopoietic stem-cell ageing. Nature, 503 (7476), 392-6.*

Core Facility

Genomics

Head of Core Facility: Prof. Dr. Christian Buske

Keywords: Microarray Analysis | Next Generation Sequencing | Data Analysis | Microarray production



Isolation of murine hematopoetic stem cells via complex multicolor FACS (Fluorescent-Activated Cell Sorting) on a BDFACSAriaIII cell-sorting machine

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The Genomics Core Facility offers several genomic services, including traditional microarray analysis as well as Next Generation Sequencing both to investigators at Ulm University as well as to external users. Established in 2001, the Genomics Core Facility started with expression and copy number microarray analyses using self-spottet Oligo- and BAC arrays (Gene Machines Omnigrid Spotter). At the time, the Genomics Core Facility was especially engaged in the development of Matrix-CGH in close collaboration with the German Cancer Research Center, Heidelberg.

In 2006 the Genomics Core Facility acquired an Affymetrix GCS 3000 system and expanded its services with the complete range of analyses offered by Affymetrix. The Genomics Core Facility is especially focused on copy number analysis in different tumor types using Affymetrix SNP arrays, and on supporting international and collaborative projects.

In 2013 the range of applications was expanded to Next Generation Sequencing by using a state-of-the-art Illumina HiSeq2000 machine. In its first year the machine was used by more than eight groups on campus that have fostered research in the fields of cancer, stem cell biology, microbiology, virology and cardiology.

The core facility currently offers a broad range of applications :

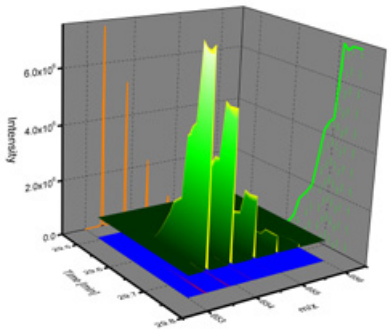
Microarray Analysis
- Expression profiling
- miRNA analyses
- SNP/Copy number analyses
- ChIP on Chip Analyses

Next Generation Sequencing
- Whole Genome Sequencing
- Exom Sequencing
- RNA Sequencing
- miRNA Sequencing
- ChIP Sequencing

Customer support includes complete assistance from sample preparation to data analysis in close collaboration with the group of H. Kestler at the Department of Bioinformatics (http://sysbio.uni-ulm.de/?Research).

Selected Publications:

- *Pannicke U, Baumann B, Fuchs S, Henneke P, Rensing-Ehl A, Rizzi M, Janda A, Hese K, Schlesier M, Holzmann K, Borte S, Laux C, Rump EM, Rosenberg A, Zelinski T, Schrezenmeier H, Wirth T, Ehl S, Schroeder ML, Schwarz K. Deficiency of innate and acquired immunity caused by an IKBKB mutation. N Engl J Med. 2013 Dec 26;369(26):2504-14.*
- *Flossbach L, Holzmann K, Mattfeldt T, Buck M, Lanz K, Held M, Möller P, Barth TF. High-resolution genomic profiling reveals clonal evolution and competition in gastrointestinal marginal zone B-cell lymphoma and its large cell variant. Int J Cancer. 2013 Feb 1;132(3):E116-27.*
- *Kuehner S, Holzmann K, Speit G. Characterization of formaldehyde's genotoxic mode of action by gene expression analysis in TK6 cells. Arch Toxicol. 2013 Nov;87(11):1999-2012.*
- *Edelmann J, Holzmann K, Miller F, Winkler D, Bühler A, Zenz T, Bullinger L, Kühn MW, Gerhardinger A, Bloehdorn J, Radtke I, Su X, Ma J, Pounds S, Hallek M, Lichter P, Korbel J, Busch R, Mertens D, Downing JR, Stilgenbauer S, Döhner H. High-resolution genomic profiling of chronic lymphocytic leukemia reveals new recurrent genomic alterations. Blood. 2012 Dec 6;120(24):4783-94.*
- *Sander S, Calado DP, Srinivasan L, Köchert K, Zhang B, Rosolowski M, Rodig SJ, Holzmann K, Stilgenbauer S, Siebert R, Bullinger L, Rajewsky K. Synergy between PI3K signaling and MYC in Burkitt lymphomagenesis. Cancer Cell. 2012 Aug 14;22(2):167-79.*



3D-plot of a doubly charged peptide from a tryptic digest of bovine serum albumin as observed during LC/MS-analysis.

Core Unit

Mass Spectrometry and Proteomics

Head of Core Unit: Dr. Sebastian Wiese

Keywords: Proteomics | Mass Spectrometry | quantitative | PTM analysis

The Core Unit of Mass Spectrometry and Proteomics (CUMP) is the most recent addition to the Medical Faculty's core facilities. The services, offered to all interested scientists, cover all aspects of proteomic research, from assistance during the initial planning phase, to sample preparation and sample fractionation, and to mass spectrometric analysis and subsequent statistical and bioinformatic analysis of primary data and downstream functional changes.

CUMP currently operates a Thermo Scientific LTQ Orbitrap Velos Pro mass spectrometer (MS) online coupled to a Dionex RSLCnano liquid chromatography (LC) system. In addition, a multi-dimensional LC system is used for SCX-driven peptide fractionation. This instrumentation allows state-of-the-art proteomic research, allowing the parallel identification and quantification of thousands of proteins.

The use of a broad range of quantitative proteomic techniques, such as SILAC (stable isotope labeling of amino acids in cell culture), label-free analyses, and isobaric tags, allows the elucidation of protein dynamics in a broad range of medical and biological fields. By using specific peptide enrichment, such as TiO_2-enrichment of phosphorylated peptides, CUMP is able to qualitatively and quantitatively analyze a number of various post-translational modifications (PTMs) and thus to shed light on cellular events involving protein processing.



In addition to the described methods, CUMP maintains a close collaboration with all scientists involved in order to devise novel solutions to newly arising questions.

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Selected Publications:

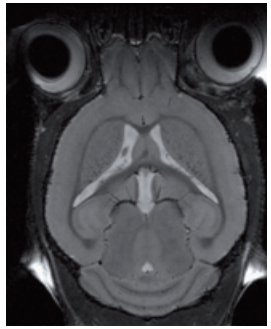
- *Gronemeyer, T., Wiese, S., Ofman, R., Bunse, C., Pawlas, M., Hayen, H., Eisenacher, M., Stephan, C., Meyer, H. E., Waterham, H. R., Erdmann, R., Wanders, R. J., and Warscheid, B. (2013): The proteome of human liver peroxisomes: identification of five new peroxisomal constituents by a label-free quantitative proteomics survey. PLoS. One. 8, e57395.*
- *Niemann, M., Wiese, S., Mani, J., Chanfon, A., Jackson, C., Meisinger, C., Warscheid, B., and Schneider, A. (2013): Mitochondrial outer membrane proteome of Trypanosoma brucei reveals novel factors required to maintain mitochondrial morphology. Mol. Cell Proteomics. 12, 515-528.*
- *Qiu, J., Wenz, L. S., Zerbes, R. M., Oeljeklaus, S., Bohnert, M., Stroud, D. A., Wirth, C., Ellenrieder, L., Thornton, N., Kutik, S., Wiese, S., Schulze-Specking, A., Zufall, N., Chacinska, A., Guiard, B., Hunte, C., Warscheid, B., van der Laan, M., Pfanner, N., Wiedemann, N., and Becker, T. (2013): Coupling of mitochondrial import and export translocases by receptor-mediated supercomplex formation. Cell 154, 596-608.*



Quantitative evaluation of a cardiac functional examination in a mouse model.



High-resolution µCT bone imaging.



High-resolution T2-weight magnetic resonance imaging of a mouse brain.

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Core Facility

Small Animal Imaging

Head of Core Facility: Prof. Dr. Volker Rasche

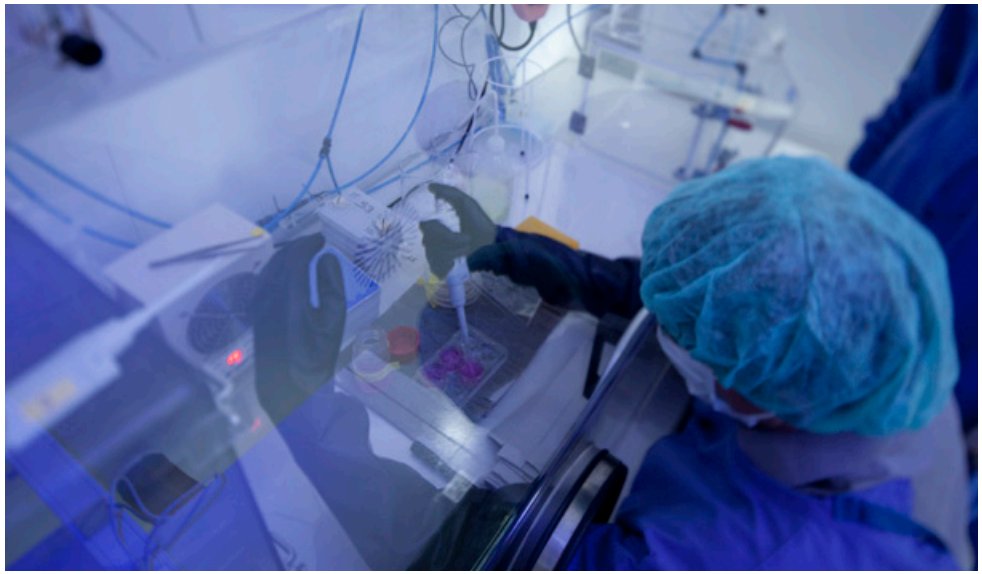
Keywords: Small animal imaging | magnetic resonance imaging | magnetic resonance spectroscopy | computer tomography

The mission of the core facility of Small Animal Imaging (SANI) is to provide a dynamic and productive environment for researchers at Ulm University, for collaborating research groups at other institutions, and for industrial partners to peform non-invasive imaging of small animals. There are currently two PhDs and one technician active at the facility and these are supported by a variety of other PhD and master students. The facility offers guidance for the planning and implementation of small animal imaging experiments by supporting applications for approval from relevant authorities and by providing the means for the post-processing and evaluation of images. Further activities include research for advanced imaging methods as well as advanced applications of MRI and MRS for the investigation of new fields in biomedical research.

The facility offers the latest technology in small animal MRI imaging and spectroscopy as well as dedicated small animal computer tomography imaging. It operates an ultrahigh field 11.7T MR imaging and spectroscopy system (BioSpec 117/16) equipped with high-sensitive cryogenically cooled receive coils and multi-channel capability. It provides technology for neurology, abdominal and thoracic imaging (MRI) in mice, rats and tissue samples. The means for physiological gating enables high-quality quantification of cardiac and other functional parameters. Advanced rapid MR spectroscopy (MRS) facilitates the study of a multitude of metabolic processes. Target nuclei include 1H, 13C, 19F, 23Na, and 31P. For X-ray imaging, mice and rats can further be scanned by µ-CT (GE eXplore Locus) and this provides the means for high-resolution anatomic imaging of, for example, bones or lung parenchyma. Animal facilities are also provided for longitudinal studies.

Selected Publications:

- *Vernikouskaya I, Fekete N, Erle A, Bannwarth M, Landfester K, Rojewski M, Schnmidtke-Schrezenmeier G, Schrezenmeier H, Rasche V. Iron-loaded PLLA (iPLLA) Nanoparticles as Highly Efficient Intracellular Markers for Visualization of Mesenchymal Stromal Cells by MRI. Contrast Media Mol Imaging. 2014 Mar-Apr;9(2):109-21.*
- *Mueller HP, Vernikouskaya I, Kassubek J, Ludolph AC, Stller D, Rasche V. Diffusion tensor magnetic resonance imaging of the brain in APP transgenic mice: a cohort study. PlosOne 2013;8(6):e67630.*
- *Martins VC, Busch K, Juraeva D, Blum C, Ludwig C, Rasche V, Lasitschka F, Mastitsky S, Brors B, Hielscher T, Fehling HJ, Rodewald HR. Cell competition is a tumour suppressor mechanism in the thymus. Nature 2014, Nature. 2014 May 22;509(7501):465-70.*
- *Weiger M, Pruessmann KP, Bracher AK, Köhler S, Lehmann V, Wolfram U, Hennel F, Rasche V. High-resolution ZTE imaging of human teeth. NMR Biomed. 2012;25(10):1144-51.*
- *Begus-Nahrmann Y, Hartmann D, Kraus J, Scheffold A, Grieb M, Rasche V, Schirmacher P, Lee HW, Kestler H, Lechel A, Rudolph KL. Transient telomere dysfunction induces chromosomal instability and promotes carcinogenesis in telomerase-proficient mice. J Clin Invest. 2012;122(6):2283-8.*



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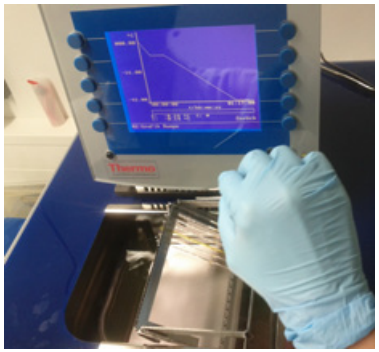
Core Facility

Transgenic Mice

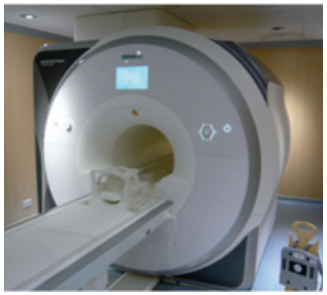
Head of Core Facility: Prof. Dr. Thomas Wirth/Mrs. Olena Sakk

Keywords: Embryo transfer | cryoconservation | pronucleus injection | in vitro fertilization



Embryofreezing

The technical manager of this core facility, which was established in July 2011, is Olena Sakk. The facility offers standard mouse technologies such as embryo transfer for hygienic sanitation, cryoconservation and the revitalization of embryos, in vitro fertilization, oophorectomy, and the generation of novel transgenic mouse lines by pronucleus injection. In addition, novel techniques, such as sperm freezing, are currently being established. The facility is supported by core funding from the Medical Faculty and thereby allows us to offer services to the researchers at Ulm University at competitive prices. In addition, services are available for external users. There has been a constant increase in demand of services from the core facility and as a consequence the facility is currently approaching its full capacity.



Front view of the new 3 Tesla whole-body magnetic resonance scanner harbored in the HF-cabin in the basement of the Department of Psychiatry.

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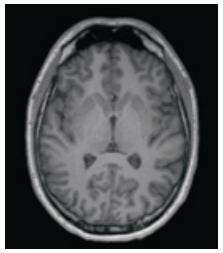
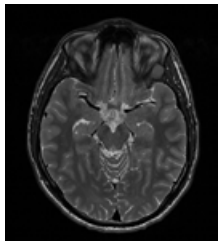
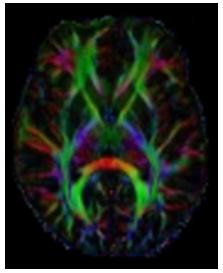


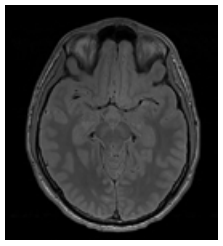
High resolution 3-dimensional T1 weighted brain image of a young male volunteer.



High resolution 3-dimensional T2 weighted brain image of a young male volunteer.



Colored fractional anisotropy mapping of a young male volunteer.



Proton density weighted brain image of a young male volunteer.

Core Facility

3 Tesla MR Imaging in Human Neuroscience

Head of Core Facility: Prof. Dr. Georg Grön

Keywords: Magnetic resonance imaging (MRI) | fMRI | perfusion MRI | structural MRI | diffusion MRI

In December 2014 the new core facility for magnetic resonance imaging in human neuroscience was established to run a new state-of-the-art 3 Tesla whole-body magnetic resonance scanner and is dedicated to research in the field of human neuroscience. The new Siemens MAGNETOM Prisma was funded equally by the German Research Foundation (*Deutsche Forschungsgemeinschaft, DFG*) and the Medical Faculty of Ulm University. The system is located in the basement of the Department of Psychiatry at Ulm University.

The mission of the core facility is to provide a campus-wide, efficient and scientific environment for research groups at Ulm University that is also open to collaborating research groups from other federal institutions as well as industrial partners. The core facility works in close collaboration with the departments of Neurology and Radiology of Ulm Medical Faculty.

The new MR scanner offers the latest technology in human brain imaging and is equipped with 20-channel and 64-channel head coils for fast parallel imaging in combination with an outstanding gradient system for high performance even under prolonged high-strain conditions. The facility provides the opportunity for in vivo brain imaging at high anatomical resolution. In particular, brain imaging under functional challenges either with “classical” BOLD (blood oxygen level dependent) or MR-based perfusion imaging by means of arterial spin labeling techniques can be provided by the facility. Several MR compatible devices for visual, acoustic and haptic stimulation are available in addition to devices that collect the responses of subjects during fMRI. The infrastructure has also been designed to run complex and elaborate pharmacological fMRI studies.

Selected Publications:

- *Ulrich M, Keller J, Hoenig K, Waller C, Grön G (2014): Neural correlates of experimentally induced flow experiences. Neuroimage, 86:194-202.*
- *Fladung AK, Schulze UM, Schöll F, Bauer K, Grön G (2013): Role of the ventral striatum in developing anorexia nervosa. Transl Psychiatry, 3:e315.*
- *Abler B, Grön G, Hartmann A, Metzger C, Walter M (2012): Modulation of frontostriatal interaction aligns with reduced primary reward processing under serotonergic drugs. J Neurosci., 32:1329-35.*
- *Cárdenas-Morales L, Grön G, Kammer T (2011): Exploring the after-effects of theta burst magnetic stimulation on the human motor cortex: a functional imaging study. Hum Brain Mapp, 32:1948-60.*
- *Graf H, Abler B, Freudenmann R, Beschoner P, Schaeffeler E, Spitzer M, Schwab M, Grön G (2011): Neural correlates of error monitoring modulated by atomoxetine in healthy volunteers. Biol Psychiatry, 69:890-7.*



Research Centers

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Molecular Mechanisms of Aging and Age-associated Diseases

Aging, Stem Cell Aging, Signal Transduction Pathways, Apoptosis

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Funded by the German Research Foundation (DFG)

KFO 167 – Regulation of Apoptosis and its Dysfunction in Human Diseases 30
Funded by the German Research Foundation (DFG)

GRK 1789 – CEMMA: Cellular and Molecular Mechanisms in Aging 31
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Funded by the German Federal Ministry of Education and Research (BMBF)

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Funded by the German Federal Ministry of Education and Research (BMBF)

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Helmholtz Virtual Institute: Resistance to Apoptosis and Therapy in Leukemia 39
Funded by the Helmholtz Association

Comprehensive Cancer Center Ulm (CCCU) 40
Funded by German Cancer Aid

Research Consortium Tumor Stem Cells 41
Funded by German Cancer Aid

Rare Neurodegenerative Diseases

German Frontotemporal Lobar Degeneration Consortium: FTLD-C 42
Funded by the German Federal Ministry of Education and Research (BMBF)

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Funded by Baden-Württemberg Foundation

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Trauma Research (physical and psychic)/ Musculoskeletal Research

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Funded by the German Research Foundation (DFG)

KFO 200 – Inflammatory Response following Musculo-Skeletal Trauma 50
Funded by the German Research Foundation (DFG)

FOR 793 – Mechanisms of Fracture Healing and Bone Regeneration in Osteoporotic Bone 51
Funded by the German Research Foundation (DFG)

Collaborative Project CANMANAGE: Case Management in Child Abuse and Neglect 52
Funded by the German Federal Ministry of Education and Research (BMBF)

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Funded by the German Federal Ministry of Education and Research (BMBF)

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Funded by the State of Baden-Württemberg

Competence Center Child Abuse and Neglect 55
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Center of Medicine and Society 59
Funded by the State of Baden-Württemberg



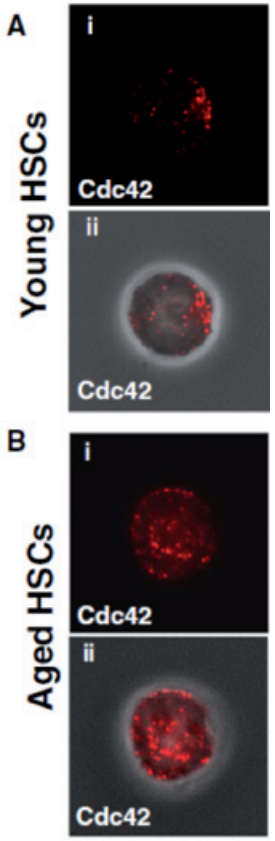
Research Centers

Ulm University Medicine has a strong scientific profile in the following main areas:

- **Molecular Mechanisms of Aging and Age-associated Diseases**
  - Aging, Stem Cell Aging, Signal Transduction Pathways, Apoptosis
  - Hemato-Oncology
  - Rare Neurodegenerative Diseases
  - Cardiometabolic Diseases (Diabetes and Obesity)
- **Trauma Research (physical and psychic)/Musculoskeletal Research**
- **Cross-sectional Centers**
- **Additional Topics**

These research topics are based on several collaborative research networks funded by a variety of funding agencies such as: the German Research Foundation (*Deutsche Forschungsgemeinschaft, DFG*); the Excellence Initiative of the German federal and state governments (*Exzellenzinitiative des Bundes und der Länder*); the Federal Ministry of Education and Research (*Bundesministerium für Bildung und Forschung, BMBF*); the European Union (EU); the State of Baden-Württemberg; and the Helmholtz Association. Funding is also received from such foundations as German Cancer Aid (*Deutsche Krebshilfe*), the *Else Kröner-Fresenius-Stiftung* or the CHDI Foundation (USA). The scientific activities of these research networks are described on the pages below.

In addition to the collaborative research networks described in this chapter, Ulm University Medicine harbors several programs dealing primarily with the promotion of young scientists. These are financed mainly by the Excellence Initiative of the German federal and state governments, the German Research Foundation and foundations such as the *Else Kröner-Fresenius-Stiftung* as described in the chapter on the *Promotion of Young Scientists* (see page 61).



Increased activity of Cdc-42 correlates with a depolarized phenotype in hematopoietic stem cells.
Representative pictures of the small RhoGTPase Cdc-42 reveal differences in distribution and activity in young (A) and old (B) hematopoietic stem cells shown on dark background (i) or as overlap with phase contrast picture (ii)
[Cell Stem Cell 10:520, 2012].

Molecular Mechanisms of Aging and Age-associated Diseases

Aging, Stem Cell Aging, Signal Transduction Pathways, Apoptosis

KFO 142 – Molecular and Cellular Aging – from Mechanisms to Clinical Perspectives

Funded by the German Research Foundation (DFG)

Speaker: Prof. Dr. Karin Scharffetter-Kochanek, Department of Dermatology and Allergic Diseases
Scientific Leader: Prof. Dr. Hartmut Geiger, Institute of Molecular Medicine
Keywords: Aging | immune system | neuron | skin | stem cells

The age-associated increase in morbidity and mortality correlates with a reduction in organ function. It is known that the intrinsic and extrinsic processes influencing aging in organs are regulated through genetic as well as a variety of environmental factors. The main aim of the clinical research group KFO 142 is to better characterize the molecular mechanisms of cellular aging inside organs and to determine the relevance of these mechanisms for the more complex in vivo situation. We will use this knowledge to develop preventative and therapeutic strategies to allow "healthy aging."

This clinical research group investigates aging processes in multiple organ systems with the initial emphasis on the immune system as well as on those systems with a likely pacemaker function for the aging of all organs (stem cells, central nervous system) or on model systems for connective tissue (skin). Research within this clinical research group will thus increase our understanding of aging-related mechanisms which alter immune system function, degeneration of central nervous system neurons, tissue regeneration (stem cells) and aging-related changes in connective tissues, including impaired wound healing.

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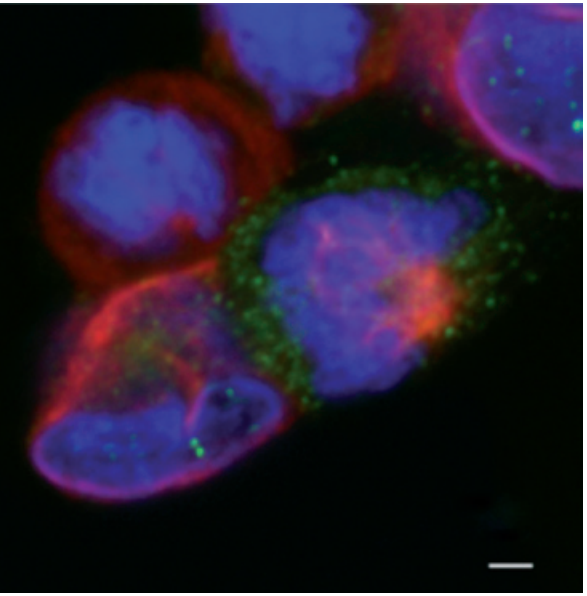
www.alternsforschung-kfo142.de/Eindex.html

Selected Publications:

- *Florian MC, Nattamai KJ, Dörr K, Marka G, Uberle B, Vas V, Eckl C, Andrä I,Schiemann M, Oostendorp RA, Scharffetter-Kochanek K, Kestler HA, Zheng Y, Geiger H. (2013) A canonical to non-canonical Wnt signalling switch in haematopoietic stem-cell ageing. Nature. 503:392-6*
- *Wang J, Sun Q, Morita Y, Jiang H, Gross A, Lechel A, Hildner K, Guachalla LM,Gompf A, Hartmann D, Schambach A, Wuestefeld T, Dauch D, Schrezenmeier H, Hofmann WK, Nakauchi H, Ju Z, Kestler HA, Zender L, Rudolph KL. (2012) A differentiation checkpoint limits hematopoietic stem cell self-renewal in response to DNA damage. Cell. 148:1001-14.*
- *Treiber N, Maity P, Singh K, Kohn M, Keist AF, Ferchiu F, Sante L, Frese S, Bloch W, Kochanek S, Sindrilaru A, Iben S, Högel J, Ohnmacht M, Claes LE, Ignatius A, Chung JH, Lee MJ, Kamenisch Y, Berneburg M, Nikolaus T, Braunstein K, Sperfeld AD, Ludolph AC, Briviba K, Wlaschek M, Scharffetter-Kochanek K. (2011) Accelerated aging phenotype in mice with conditional deficiency for mitochondrial superoxide dismutase in the connective tissue. Aging Cell. 10:239-254.*



Abnormally dividing neuroblastoma cells about to undergo apoptosis after treatment with a novel anti-cancer drug.

Molecular Mechanisms of Aging and Age-associated Diseases

Aging, Stem Cell Aging, Signal Transduction Pathways, Apoptosis

KFO 167 – Regulation of Apoptosis and its Dysfunction in Human Diseases

Funded by the German Research Foundation (DFG)

Speaker: Prof. Dr. Klaus-Michael Debatin, Department of Pediatrics and Adolescent Medicine

Head: Prof. Dr. Christian Beltinger, Department of Pediatrics and Adolescent Medicine

Keywords: apoptosis | cancer | HIV infection | DNA damage | signal transduction

Apoptosis is the major form of cell death in humans and is thus tightly regulated. Too much apoptosis causes disease, as, for example, in HIV infection, tissue injury or neurodegeneration. Too little apoptosis, as in cancer, is also detrimental. Although the molecular basis of apoptosis is increasingly understood, the clinical translation of this knowledge remains a challenge. The DFG-funded clinical research unit “Regulation of Apoptosis and its Dysfunction in Human Diseases” addresses this challenge by bringing together eight apoptosis research projects that focus on human disease in the areas of cancer, infection and aging. By forming an interdisciplinary consortium, both preclinical-theoretical institutes (Legal Medicine, Molecular Medicine, Physiological Chemistry, and Molecular Virology) and clinical departments of the Medical Faculty (Pediatrics and Adolescent Medicine, Internal Medicine III and the Section of Gynecological Oncology) have joined forces in research with the ultimate aim of benefitting patients.

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Selected Publications:

- *Laguette N, Brégnard C, Hue P, Basbous J, Yatim A, Larroque M, Kirchhoff F, Constantinou A, Sobhian B, Benkirane M. Premature activation of the SLX4 complex by Vpr promotes G2/M arrest and escape from innate immune sensing. Cell 2014; 156(1-2): 134-145.*
- *Sperka T, Song Z, Morita Y, Nalapareddy K, Guachalla LM, Lechel A, Begus-Nahrmann Y, Burkhalter MD, Mach M, Schlaudraff F, Liss B, Ju Z, Speicher MR, Rudolph KL. Puma and p21 represent cooperating checkpoints limiting self-renewal and chromosomal instability of somatic stem cells in response to telomere dysfunction. Nat Cell Biol. 2011; 14:73-79.*
- *Meyer LH, Eckhoff SM, Queudeville M, Kraus JM, Giordan M, Stursberg J, Zangrando A, Vendramini E, Möricke A, Zimmermann M, Schrauder A, Lahr G, Holzmann K, Schrappe M, Basso G, Stahnke K, Kestler HA, Te Kronnie G, Debatin KM. Early relapse in ALL is identified by time to leukemia in NOD/SCID mice and is characterized by a gene signature involving survival pathways. Cancer Cell 2011; 19:206-217.*



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Molecular Mechanisms of Aging and Age-associated Diseases

Aging, Stem Cell Aging, Signal Transduction Pathways, Apoptosis

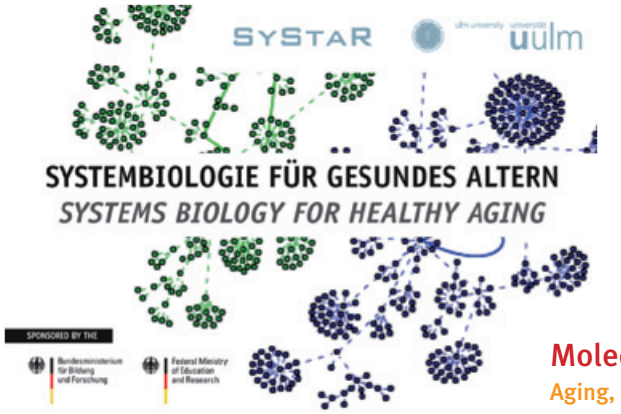
GRK 1789 – CEMMA: Cellular and Molecular Mechanisms in Aging

Funded by the German Research Foundation (DFG)

Speaker: Prof. Dr. Hartmut Geiger, Institute of Molecular Medicine

Keywords: aging | stem cells | cancer | neurodegenerative diseases | immunology

Demographic development predicts an inversion of the demographic structure in most Western societies over the coming decades that will result in a significant increase in age-associated diseases. These diseases and their prevention will become a key focus of medicine, business and social studies. Improved knowledge of the molecular and cellular mechanisms of aging will allow rational approaches and therapies to be devised that are ultimately aimed at achieving healthy aging. The research training program known as “Cellular and Molecular Mechanisms in Aging” (CEMMA) will recruit and train the next generation of scientists engaged in aging research, a very critical task in light of anticipated demographic development. CEMMA has been designed as a structured and internationally recognized training program for doctoral students working in the field of aging research. The qualification program on aging research includes specific teaching modules on model systems in aging research and on the theories of molecular aging in addition to modules analyzing aging in the context of general medicine and social studies. CEMMA works closely together with the International Graduate School in Molecular Medicine Ulm.



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Molecular Mechanisms of Aging and Age-associated Diseases

Aging, Stem Cell Aging, Signal Transduction Pathways, Apoptosis

Collaborative Project SyStaR – Molecular Systems Biology of Impaired Stem Cell Function and Regeneration during Aging

Funded by the German Federal Ministry of Education and Research (BMBF)

Speakers: Prof. Dr. Karin Scharffetter-Kochanek, Department of Dermatology and Allergic Diseases
PD Dr. Hans Kestler, Friedrich-Schiller University Jena
Prof. Dr. Hartmut Geiger, Institute of Molecular Medicine

Keywords: Molecular Systems Biology | Stem Cells | Aging | Regeneration

Aging-associated decreases in regenerative capacity and organ maintenance represent major factors limiting the quality of life during aging. It is assumed that limiting self-renewal and function of adult stem cells or the regenerative reserve of somatic organ cells are major underlying causes of tissue aging. To this end, an interdisciplinary research team will analyze age-related alterations in stem cell compartments and regenerative tissues of model organisms, in genetic mouse models of aging and in humans. Systems biology analysis will be used to generate mathematical models on aging-associated alteration in signaling pathways that are relevant to human aging. Functional analysis and validation of the generated models will be conducted in model organisms and in genetic mouse models, thereby inducing an iterative process of model optimization and experimental re-evaluation.

The SyStaR consortium will identify functionally relevant signaling pathways, contributing to a decline in stem cell function and regeneration during human aging. SyStaR will determine whether identified signaling pathways can serve as therapeutic targets for treatment or prevention of regenerative dysfunction and impaired organ maintenance during human aging.

Prof. Dr. Scharffetter-Kochanek (clinic), Prof. Dr. Hartmut Geiger (basic research and life sciences) und PD Dr. Kestler (systems biology) coordinate SyStaR.

Selected Publications:

- *L. Lausser, C. Müssel, M. Maucher, and H.A. Kestler (2013): Measuring and visualizing the stability of biomarker selection techniques. Computational Statistics, 28(1).*
- *Florian MC, Nattamai KJ, Dorr K, Marka G, Uberle B, Vas V, Eckl C, Andra I, Schiemann M, Oostendorp RA, Scharffetter-Kochanek K, Kestler HA, Zheng Y, Geiger H (2013): A canonical to non-canonical Wnt signaling switch in haematopoietic stem-cell aging. Nature, 503(7476):392-396.*
- *J. Wang, Q. Sun, Y. Morita, H. Jiang, A. Groß, A. Lechel, K. Hildner, L. M. Guachalla, A. Gompf, D. Hartmann, A. Schambach, T. Wuestefeld, D. Dauch, H. Schrezenmeier, W. Hofmann, H. Nakauchi, Z. Ju, H. A. Kestler, L. Zender, and K. L. Rudolph (2013): A Differentiation Checkpoint Limits Hematopoietic Stem Cell Self-Renewal in Response to DNA Damage. Cell, 148(5):1001–1014.*

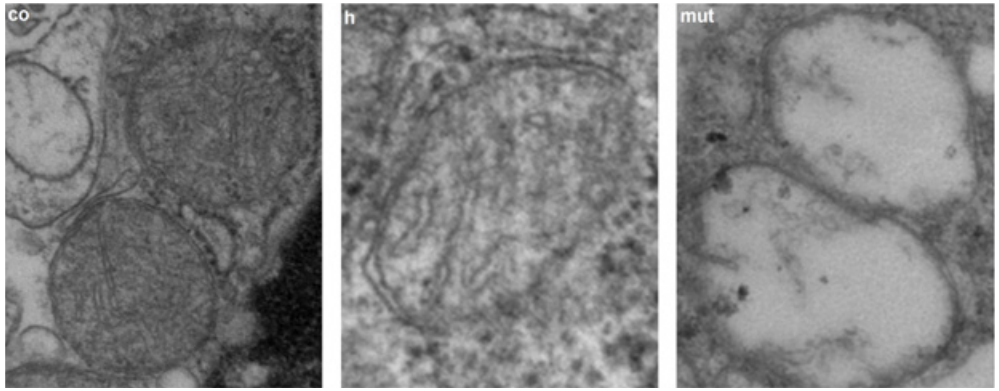

Fig.1 Oxidative damage within mitochondria of manganese superoxide dismutase deficient skin fibroblasts. Transmission electron microscopy and assessment of mitochondria revealed a severely disturbed structure with loss of cristae and degeneration of intramitochondrial structure in more than 80% of all assessed mitochondria in manganese superoxide dismutase (Sod2) deficient mutant fibroblasts (mut) compared with 40% damaged mitochondria in Sod2 heterozygous (h) and only 5% in wild type Sod2-competent fibroblasts (co).

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Molecular Mechanisms of Aging and Age-associated Diseases

Aging, Stem Cell Aging, Signal Transduction Pathways, Apoptosis

Center of Cellular Decision and Signaling Pathways during Aging – From Mechanisms to Clinical Perspectives

funded by the State of Baden-Württemberg

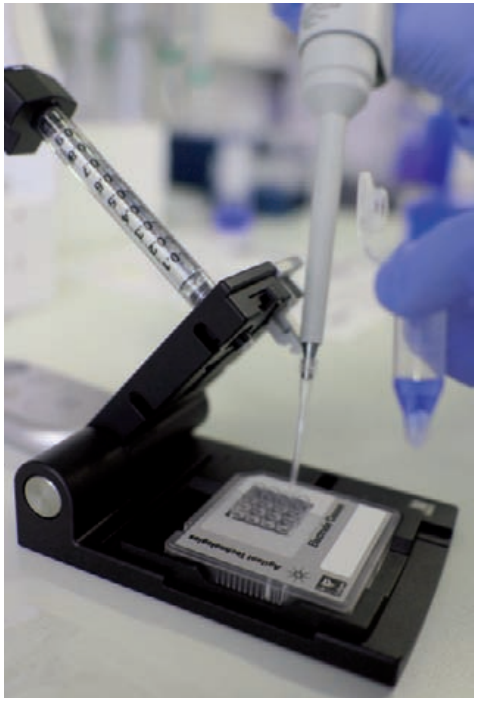
Speaker: Prof. Dr. Karin Scharffetter-Kochanek, Department of Dermatology and Allergic Diseases

Keywords: Aging | Aging associated-diseases | Molecular and cellular Mechanisms of Aging | Signaling pathways

Major research efforts will be required to successfully meet the urgent challenges of current demographic development. Aging is defined as a progressive loss of function with a gradual increase in frailty, morbidity and mortality. Aging research within this collaborative program aims to advance our mechanistic understanding of the cellular and molecular processes of intrinsic aging and how this relates to aging-associated diseases, including infectious diseases, autoimmunity, impaired tissue regeneration, degenerative disorders and cancer. Major questions address stem cell exhaustion in different tissues with lack of tissue regeneration and anti-aging pathways, including the IGF-1, Wnt-, Notch- and stress response pathways. Functional analysis of key-regulatory components have already been identified and we will further identify biomarkers and target molecules to monitor and delay aging and aging-related diseases with the ultimate goal of promoting healthy aging for the benefit of all our patients. Due to the unique interaction of basic, translational and clinical research with the opportunities for novel targeted strategies, this research center will further enhance the internationally recognized profile of aging research at Ulm.

Selected Publications:

- *Koch S, Garcia Gonzalez O, Assfalg R, Schelling A, Schäfer P, Scharffetter-Kochanek K, Iben S. (2014) Cockayne syndrome protein A is a transcription factor of RNA polymerase I and stimulates ribosomal biogenesis and growth. Cell Cycle. Apr 29;13(13). [Epub ahead of print]*
- *Florian MC, Nattamai KJ, Dörr K, Marka G, Uberle B, Vas V, Eckl C, Andrä I,Schiemann M, Oostendorp RA, Scharffetter-Kochanek K, Kestler HA, Zheng Y, Geiger H. (2013) A canonical to non-canonical Wnt signalling switch in haematopoietic stem-cell ageing. Nature. 503:392-6.*
- *Florian MC, Dörr K, Niebel A, Daria D, Schrezenmeier H, Rojewski M, Filippi MD, Hasenberg A, Gunzer M, Scharffetter-Kochanek K, Zheng Y, Geiger H. (2012) Cdc42 Activity Regulates Hematopoietic Stem Cell Aging and Rejuvenation. Cell Stem Cell 10:520-530.*



Molecular Mechanisms of Aging and Age-associated Diseases

Aging, Stem Cell Aging, Signal Transduction Pathways, Apoptosis

Else Kröner Research College Ulm – Stem Cells, Aging and Malignant Transformation: From Experimental Models to Clinical Application

funded by the Else Kröner-Fresenius-Stiftung

Speakers: Prof. Dr. Stephan Stilgenbauer, Department of Internal Medicine III
Prof. Dr. Hartmut Geiger, Institute of Molecular Medicine

Keywords (up to five): Stem cells | aging, malignant transformation | physician scientist | career development

The Else Kröner Forschungskolleg Ulm is a structured postgraduate training program for highly talented junior physicians in the phase of clinical specialization. It is financially supported through a research grant from the Else Kröner-Fresenius-Stiftung. It facilitates scientific career development by freeing junior physicians from clinical duties and allowing them to fully dedicate their time for scientific projects. The scientific theme of the Forschungskolleg is "stem cells, aging and malignant transformation," a research priority of Ulm University with a documented track record in publications and research grant funding. The Forschungskolleg is an autonomous structure with its own budget and is based on participating institutions and clinical departments. It is structurally embedded in the Medical Faculty and the University Medical Center of Ulm University. The promotion of scientific career development is a key topic and is supported by Ulm University as one of its ultimate goals. The selection procedure of the participants involves a structured application process that outlines their research project within a mentoring concept. The support of the clinical department must be documented through a commitment statement issued by its medical director. In addition to scientific research, there is a structured mentoring concept that allows the development of individual career perspectives. Therefore, each participant is supported in such a way to develop their personal integrated concept of research and clinical training. The ultimate goal of the Else-Kröner Forschungskolleg Ulm is to support junior physicians in pursuit of a career as a "physician scientist" within a truly translational concept that combines basic scientific research and clinical application. The Else-Kröner Forschungskolleg Ulm was initiated in 2011 and has supported ten participants who have so far authored 41 original reports and eight reviews in international journals.

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Selected Publications:

- *Reduction of CD18 promotes expansion of inflammatory γδ T cells collaborating with CD4+ T cells in chronic murine psoriasiform dermatitis. Gatzka M, Hainzl A, Peters T, Singh K, Tasdogan A, Wlaschek M, Scharffetter-Kochanek K. J Immunol. 2013, 191(11):5477-88.*
- *NOTCH1, SF3B1, and TP53 mutations in fludarabine-refractory CLL patients treated with alemtuzumab: results from the CLL2H trial of the GCLLSG Schnaiter A, Paschka P, Rossi M, Zenz T, Bühler A, Winkler D, Cazzola M, Döhner K, Edelmann J, Mertens D, Kless S, Mack S, Busch R, Hallek M, Döhner H, Stilgenbauer S. Blood. 2013, 122(7):1266-70.*
- *Rapid engraftment of human ALL in NOD/SCID mice involves deficient apoptosis signaling. Queudeville M, Seyfried F, Eckhoff SM, Trentin L, Ulrich S, Schirmer M, Debatin KM, Meyer LH. Cell Death Dis. 2012, 3:e364.*



After the signing of the agreement:
(from left to right) Prof. Dr. Klaus-Michael Debatin (speaker BIU, Head of the Department of Pediatrics and Adolescent Medicine); Prof. Dr. Andreas Barner (speaker of the Boehringer Ingelheim management); Theresia Bauer (Minister of Science, Research and the Arts of the State of Baden-Württemberg); Prof. Dr. Gerd Schnorrenberg (vice speaker of BIU and Senior Vice President of Boehringer Research Germany); and Prof. Dr. Karl-Joachim Ebeling (President of Ulm University).

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Molecular Mechanisms of Aging and Age-associated Diseases

Aging, Stem Cell Aging, Signal Transduction Pathways, Apoptosis

Boehringer Ingelheim Ulm University BioCenter (BIU)

Research Center in Public-Private Partnership

Speaker: Prof. Dr. Klaus-Michael Debatin, Department of Pediatrics and Adolescent Medicine
Vice Speaker: Prof. Dr. Gerd Schnorrenberg, Boehringer Ingelheim Pharma GmbH & Co. KG
Keywords: Cardio metabolic diseases | COPD | Neurodegenerative diseases

On 19 October 2011, Prof. Dr. Gerd Schnorrenberg, Senior Vice President of Boehringer Research Germany, and Prof. Dr. Karl Joachim Ebeling, President of Ulm University, signed the co-operation agreement for the "Public-Private Partnership research consortium Boehringer Ingelheim Ulm University BioCenter (BIU)" in the presence of Theresia Bauer, Minister of Science, Research and the Arts of the State of Baden-Württemberg, and Prof. Dr. Dr. Andreas Barner, the speaker of the Boehringer Ingelheim management.

The BioCenter includes in total 17 research projects focusing on neurodegenerative (e.g. Morbus Parkinson and Morbus Alzheimer) and cardio metabolic diseases (Adipositas, Diabetes and Cardiac Infarction)as well as lung diseases (e.g. COPD - Chronic Obstructive Pulmonary Disease). The goals of this research center are the identification and characterization of new biomarkers and the analysis of deregulated signaling pathways in diseases as well as establishing new innovative preclinical and clinical concepts in translational research. The BioCenter, which is unique in Germany because of its scientific interaction between academia and the pharmaceutical industry, has been established according to the structures and criteria of excellence stipulated by the well-established collaborative research centers of the German Research Foundation (DFG). The pharmaceutical company of Boehringer Ingelheim, the State of Baden-Württemberg and the Medical Faculty of the Ulm University support this program and have contributed €4.5 million for an initial three year period. A second three to five year funding period has also been planned.

Selected Publications:

- *Rijal Upadhaya A, Kosterin I, Kumar S, von Arnim CA, Yamaguchi H, Fandrich M, Walter J, Thal DR (2014). Biochemical stages of amyloid-beta peptide aggregation and accumulation in the human brain and their association with symptomatic and pathologically preclinical Alzheimer's disease. Brain. 137 (Pt 3): 887-903.*
- *Salem HH, Trojanowski B, Fiedler K, Maier HJ, Schirmbeck R, Wagner M, Boehm BO, Wirth T, Baumann B (2014). Long-term IKK2/NF-κB signaling in pancreatic β-cells induces immune-mediated diabetes mellitus. Diabetes. 63(3): 960-75.*
- *Zimmermann T, Berger I, Just S, Rottbauer W, Dahme T (2013). Loss of Swi/snf-complex Subunit Heart of Stone Leads to Cardiac Hyperplasia in Zebrafish. Circulation. 128: A18015.*

For more information please see the website of BIU.
http://fakultaet.medizin.uni-ulm.de/forschung/verbuende/biu/

Molecular Mechanisms of Aging and Age-associated Diseases

Hemato-Oncology

SFB 1074 – Experimental Models and Clinical Translation in Leukemia

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Funded by the German Research Foundation (DFG)

Coordinating Principal Investigator: Prof. Dr. Hartmut Döhner, Department of Internal Medicine III

Keywords: Leukemia | Malignant transformation | Genomics | Animal models | Clinical translation



Group photo of the members of the SFB1074 at the Summer 2013 retreat.

The focus of cancer drug development has shifted from conventional chemotherapy to therapeutics targeting molecular lesions of cancer cells. Despite major efforts to catalog genetic lesions that drive human cancers, a major challenge remains to integrate these findings from basic scientific research and clinical investigations in order to improve patient outcome.

The SFB1074 aims to bridge this gap in a highly focused area of cancer research, namely, acute and chronic leukemias, diseases which are most prevalent in the elderly population. Ulm University has a long-standing commitment to cutting-edge basic, translational and clinical research on hematopoietic malignancies as reflected by a large number of research groups focusing on diverse aspects of leukemia biology as well as by some of the largest biobanks and most prestigious clinical programs in this area.

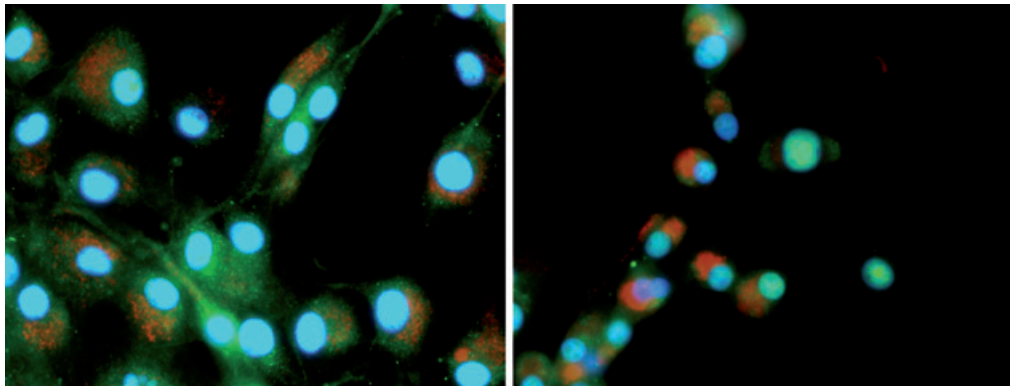
Research within the CRC is organized into two Project Groups which closely interact with each other to fully exploit the potential of combining excellent basic science with clinical expertise. Projects in Group A use a broad spectrum of physiologically relevant in vitro and in vivo experimental systems to investigate cellular and molecular mechanisms of leukemogenesis. Projects in Group B have a strong translational aspect and are aimed at the genetic, epigenetic and functional characterization of leukemia samples from patients with acute and chronic leukemia and/or human-derived experimental systems.

In summary, the SFB1074 provides a superb opportunity to realize the concept of translational research “from bench to bedside and back” in acute and chronic leukemias. It is hoped that this approach will substantially contribute to an improved understanding of leukemia biology and, more importantly, to a better clinical management of patients with these diseases.

The SFB1074 was initiated in July 2012 and has started its programs very successfully with already more than ten publications in international journals.

Selected Publications:

- *Clonal evolution in relapsed NPM1 mutated acute myeloid leukemia. Krönke J, Bullinger L, Teleanu V, Tschürtz F, Gaidzik VI, Kühn MW, Rücker FG, Holzmann K, Paschka P, Kapp-Schwörer S, Späth D, Kindler T, Schittenhelm M, Krauter J, Ganser A, Göhring G, Schlegelberger B, Schlenk RF, Döhner H, Döhner K. Blood. 2013 Jul 4;122(1):100-8. doi: 10.1182/blood-2013-01-479188. Epub 2013 May 23. PubMed PMID: 23704090.*
- *NOTCH1, SF3B1, and TP53 mutations in fludarabine-refractory CLL patients treated with alemtuzumab: results from the CLL2H trial of the GCLLSG Schnaiter A, Paschka P, Rossi M, Zenz T, Bühler A, Winkler D, Cazzola M, Döhner K, Edelmann J, Mertens D, Kless S, Mack S, Busch R, Hallek M, Döhner H, Stilgenbauer S. Blood. 2013 Aug 15;122(7):1266-70. doi: 10.1182/blood-2013-03-488197. Epub 2013 Jul 2. PubMed PMID: 23821658.*
- *Rapid engraftment of human ALL in NOD/SCID mice involves deficient apoptosis signaling. Queudeville M, Seyfried F, Eckhoff SM, Trentin L, Ulrich S, Schirmer M, Debatin KM, Meyer LH. Cell Death Dis. 2012 Aug 9;3:e364. doi: 10.1038/cddis.2012.107. PubMID: 22875001.*



After treatment with B10, key components of both the apoptosis and the lysosomal cell death signaling cascade are redistributed within the cells. Left: untreated cells; right: treated with B10.

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Molecular Mechanisms of Aging and Age-associated Diseases

Hemato-Oncology

Joint Project ApoCanBA – Targeting Apoptosis for Cancer Therapy: Preclinical and Clinical Evaluation of Betulinic Acid Derivate BA10 as a novel Lysosomotropic Anticancer Drug

Funded by the German Federal Ministry of Education and Research (BMBF)

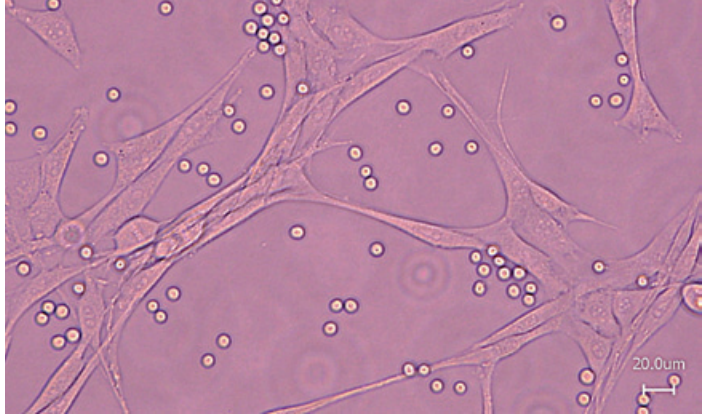
Speaker: Prof. Dr. Klaus-Michael Debatin, Department of Pediatrics and Adolescent Medicine

Keywords: Lysosomal cell death | betulinic acid | mitochondria

Despite aggressive protocols, the inefficacy of established treatments remains a major problem in oncology and highlights the need for novel strategies. In response to this demand, this consortium aims to develop betulinic acid (BA) as a novel class of anticancer drugs with a wide therapeutic index that triggers apoptosis and lysosomal membrane permeabilization, two intrinsic cell death programs. BA is a natural product extracted from the bark of the birch tree. Since it exerts its antitumor action in a manner different from conventional anticancer drugs, it is able to overcome resistance. This joint project combines the expertise of an industrial partner, a preclinical partner and a clinical partner. It aims at pharmacodynamically optimizing a BA derivative, evaluating its preclinical toxicity profile and producing it under good medical practice (GMP) conditions for evaluation in a clinical trial in malignant brain tumors.

Selected Publications:

- *Enzenmüller S, Gonzalez P, Karpel-Massler G, Debatin KM, Fulda S (2013): GDC-0941 enhances the lysosomal compartment via TFEB and primes glioblastoma cells to lysosomal membrane permeabilization and cell death. Cancer Lett 329:27-36.*
- *Gonzalez P, Mader I, Tchoghandjian A, Enzenmüller S, Cristofanon S, Basit F, Debatin KM, Fulda S (2012): Impairment of lysosomal integrity by B10, a glycosylated derivative of betulinic acid, leads to lysosomal cell death and converts autophagy into a detrimental process. Cell Death Differ 19:1337-46.*



Most tumor cells die without support from neighboring cells. When primary leukemic cells from patients (small cells) are cultured with supporting cells from the bone marrow (large cells), these interactions can be investigated in detail. Picture by Bhattacharya and Mertens. Also published in Die Zeit, 13.6.2013

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Molecular Mechanisms of Aging and Age-associated Diseases

Hemato-Oncology

Collaborative Project CancerEpiSys – Integrative Analysis of Epigenetic Networks that Determine the Chronic Lymphocytic Leukemia Disease State

Funded by the German Federal Ministry of Education and Research (BMBF)

Speakers: PD Dr. Daniel Mertens, Department of Internal Medicine III,
PD Dr. Karsten Rippe, Research Group Genome Organization and Function, DKFZ Heidelberg,

Keywords: Leukemia | Epigenetic | Microenvironment | non-coding RNA | signaling

The Cooperation Unit “Mechanisms of Leukemogenesis” integrates research in the clinical environment of Ulm University with research at the German Cancer Research Center. It is ideally suited to translate basic research towards clinical application. Examples are:

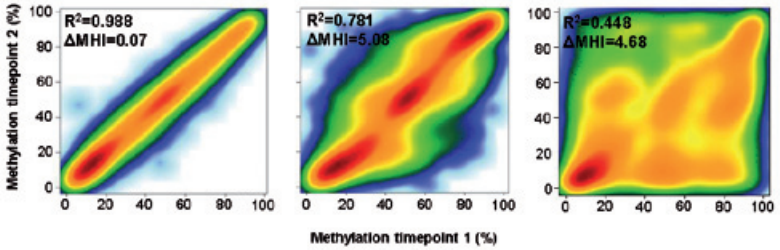
i) The detailed functional characterization of epigenetic modifications of the DNA of leukemia cells. We expect these epigenetic marks to represent the history and functional wiring of cells. This would make them ideally suited to predict the response to treatment and the clinical outcome of patients. Part of this task will be addressed in the scientific network www.cancerepisys.org.

ii) The identification of compounds that target the interaction of leukemia cells with non-malignant cells that surround them. Intriguingly, leukemic cells cannot survive without non-malignant cells. Promising substances were identified by comparing the activity of all human genes in protected and unprotected leukemic cells. Preliminary results show the suitability of this approach, which will be exploited in a Virtual Helmholtz Institute (www.leukemia-net.de).

Both approaches are only possible through the bipartite setup of the Cooperation Unit, allowing translational projects that are not feasible in either research group alone.

Selected Publications:

- *Allegra, D., Bilan, V., Garding, A., Döhner, H., Stilgenbauer, S., Kuchenbauer, F., Mertens, D. (2013), Defective DROSHA processing contributes to downregulation of miR-15/-16 in chronic lymphocytic leukemia, Leukemia, in press, IF 10.164.*
- *Garding, A., Bhattacharya, N., Claus, R., Ruppel, M., Tschuch, C., Zucknick, M., Oakes, C., Fleig, V., Allegra, D., Caudron-Herger, M., Filarsky, K., Keklikoglou, I., Serra, L., Weichenhan, D., Idler, I., Benner, A., Radlwimmer, B., Zentgraf, H., Wiemann, S., Rippe, K., Plass, C., Döhner, H., Lichter, P., Stilgenbauer, S., Mertens, D., “Epigenetic upregulation of lncRNAs at 13q14.3 in leukemia correlates with downregulation in cis of a gene cluster regulating NF-kB.”, PLoS Genetics, 9(4): e1003373., IF 8.694.*
- *Garding, A., Bhattacharya, N., Haebe, S., Mueller, F., Weichenhan, D., Idler, I., Ickstadt, K., Stilgenbauer, S. & Mertens, D. (2013) “TCL1A and ATM are coexpressed in chronic lymphocytic leukemia cells without deletion of 11q.” Haematologica, 98(2):269-73. IF 6.416.*



The epigenetic modification of DNA-methylation can remain stable in leukemic cells over time (left panel) or change (middle and right panel). Shown is the DNA-methylation level of 450.000 genomic loci at two different timepoints (x-axis vs y-axis) in three patients. These changes in DNA-methylation are correlated with the prognosis of patients and can therefore be used to predict the clinical course of the patients.

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Molecular Mechanisms of Aging and Age-associated Diseases

Hemato-Oncology

Helmholtz Virtual Institute: Resistance to Apoptosis and Therapy in Leukemia

Funded by the Helmholtz Association

Speakers: Prof. Dr. Peter Lichter, Division of Molecular Genetics, DKFZ Heidelberg,
PD Dr. Daniel Mertens, Department of Internal Medicine III

Keywords: leukemia | resistance | microenvironment | small molecule screen | signaling

A major pathomechanism and obstacle for the treatment of malignant disease is the resistance of tumor cells against apoptosis and chemotherapy. We hypothesize that cell-intrinsic as well as cell-extrinsic mechanisms, mediated by the microenvironment and the functional interplay of these pathways, contribute to the escape from cell death and to drug resistance. In order to understand the molecular mechanisms of resistance and translate them into novel treatment strategies, we use chronic lymphocytic leukemia (CLL), the most common adult leukemia in the western world, as an ideally suited model system, and expect to identify general mechanisms contributing to cancer cell resistance. The proposed institute will have access to unique primary tissue biobanks as well as compound libraries. In addition, the combination of expertise in molecular biology, state-of-the-art technology and the clinical skills of the Helmholtz Virtual Institute will allow us to put forward biologically and clinically relevant questions and to translate biological findings into clinical application.

Selected Publications:

- *Woyach. J. A., Furman, R., Liu, T.M., Ozer, H. G., Zapatka, M., Ruppert, A. S., Xue, Z., Li, D., Steggerda, S., Versele, M., Dave, S. S., Zhang, J., Yilmaz, A. S., Jaglowski, S., Blum, K. A., Lozanski, A., Lozanski, G., James, D. F., Barrientos, J., Lichter, P., Stilgenbauer, S., Buggy, J., J., Chang, B.Y., Johnson, A., J., Byrd, J. C. (2014). "Novel Recurring Resistance Mechanism for the Irreversible Bruton's Tyrosine Kinase (BTK) Inhibitor Ibrutinib", N Engl J Med, in press, IF 51.658.*
- *Garding, A., N. Bhattacharya, R. Claus, M. Ruppel, C. Tschuch, K. Filarsky, I. Idler, M. Zucknick, M. Caudron-Herger, C. Oakes, V. Fleig, I. Keklikoglou, D. Allegra, L. Serra, S. Thakurela, V. Tiwari, D. Weichenhan, A. Benner, B. Radlwimmer, H. Zentgraf, S. Wiemann, K. Rippe, C. Plass, H. Dohner, P. Lichter, S. Stilgenbauer and D. Mertens (2013). "Epigenetic upregulation of lncRNAs at 13q14.3 in leukemia is linked to the In Cis downregulation of a gene cluster that targets NF-kB." PLoS Genet 9(4): e1003373. IF 8.517.*
- *Dietrich, S., H. Glimm, M. Andrulis, C. von Kalle, A. D. Ho and T. Zenz (2012). "BRAF inhibition in refractory hairy-cell leukemia." N Engl J Med 366(21): 2038-2040. IF 51.658.*



Interdisciplinary clinical tumor conference: The CCCU promotes excellence in interdisciplinary patient care and innovative treatments as well as basic scientific and translational research in order to develop novel therapeutic approaches.

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Molecular Mechanisms of Aging and Age-associated Diseases

Hemato-Oncology

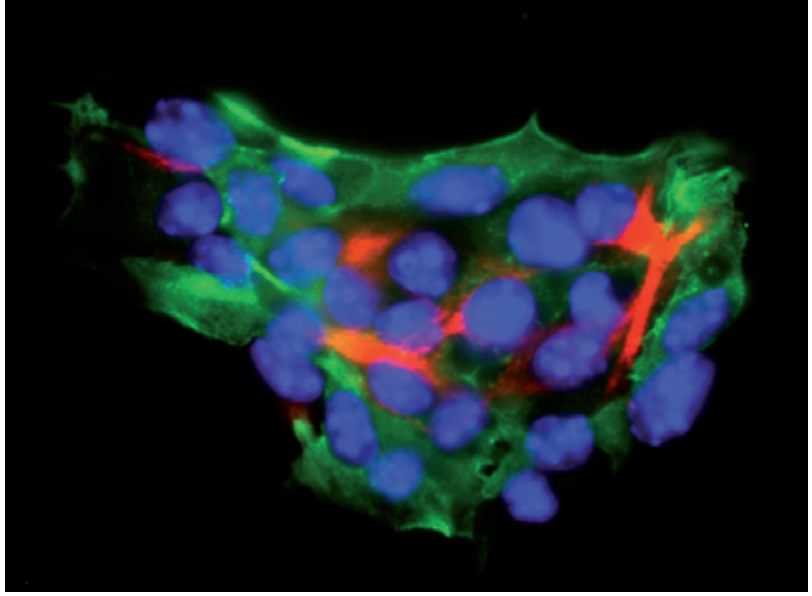
Comprehensive Cancer Center Ulm (CCCU)

Funded by German Cancer Aid

Director: Prof. Dr. Hartmut Döhner, Department of Internal Medicine III
Deputy Director: Prof. Dr. Thomas Seufferlein, Department of Internal Medicine I
Secretary: Prof. Dr. Jens Huober, Department of Gynecology and Obstetrics
Keywords: Basic and translational research | Comprehensive Cancer Center | clinical trials | phase I unit

The Comprehensive Cancer Center Ulm (CCCU) is a national interdisciplinary Oncology Center of Excellence
Board-certified consultants lead interdisciplinary teams to ensure the highest quality of patient care by organizing tumor conferences, updating standard operating procedures, supporting patient organizations, providing a consultation service for associated external partners (from private practice and hospitals), and by implementing new treatment trials.
The CCCU is committed to multidisciplinary patient care, interactive and innovative clinical and laboratory research, high activity in phase I-IV clinical trials, training for health professionals, community services as well as cancer prevention. These activities are an integral part of various national and international research networks and programs.
In addition to the research laboratories of the participating departments, the Institute of Experimental Oncology was founded within the CCCU as a driving force to promote cancer research dedicated to translating results from cancer biology into innovative therapeutic concepts. In order to establish a corporate identity of translational cancer research under the umbrella of the CCCU, the “Preclinical Cancer Center Ulm” has recently been founded.
Moreover, Ulm University has developed an international postgraduate online study program in Advanced Oncology aimed at clinical oncologists as well as scientists to promote the increased level of excellence in comprehensive care for cancer patients.

For publications please see the websites of the CCCU members.
www.ccc-ulm.de



Neural crest stem cells, shown here to differentiate, can give rise to neuroblastoma and its tumor stem cells.

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Molecular Mechanisms of Aging and Age-associated Diseases

Hemato-Oncology

Research Consortium Tumor Stem Cells

Funded by German Cancer Aid

Speaker: Prof. Dr. Christian Beltinger, Department of Pediatrics and Adolescent Medicine

Keywords: Tumor stem cells | tumor-initiating cells | cancer

Most tumors are heterogeneous and many are organized in a hierarchical fashion with so-called tumor stem cells or tumor-initiating cells giving rise to more differentiated tumor cells. The Research Consortium “Tumor Stem Cells” was founded in 2005 and is a national consortium that aims to isolate and characterize tumor stem cells in solid tumors. This consortium, financed by *Deutsche Krebshilfe* (German Cancer Aid), is currently in its final funding period. A broad spectrum of solid tumors from different organs that spans embryonic tumors to cancers in old age is investigated by several groups in Germany. The common links between the projects are to develop generic methods to enrich and isolate tumor stem cells, to find molecular mechanisms shared by the tumor stem cells of these diverse tumor entities and to define therapeutic targets within the tumor stem cells.

Selected Publications:

- *Begus-Nahrmann Y, Hartmann D, Kraus J, Eshraghi P, Scheffold A, Grieb M, Rasche V, Schirmacher P, Lee HW, Kestler HA, Lechel A, Rudolph KL. (2012) Transient telomere dysfunction induces chromosomal instability and promotes carcinogenesis. J Clin Invest,122:2283-22888.*
- *Katz SF, Lechel A, Obenauf AC, Begus-Nahrmann Y, Kraus JM, Hoffmann EM, Duda J, Eshraghi P, Hartmann D, Liss B, Schirmacher P, Kestler HA, Speicher MR, Rudolph KL. (2012) Disruption of Trp53 in livers of mice induces formation of carcinomas with bilineal differentiation. Gastroenterology, 142:1229-1239.*
- *Petersson M, Brylka H, Kraus A, John S, Rappl G, Schettina P, and Niemann C (2011) TCF/Lef1 activity controls establishment of diverse stem and progenitor cell compartments in mouse epidermis. The EMBO Journal, 30: 3004–3018.*

Map of FTLD-C locations in Germany



Molecular Mechanisms of Aging and Age-associated Diseases

Rare Neurodegenerative Diseases

German Frontotemporal Lobar Degeneration Consortium: FTLD-C

Funded by the German Federal Ministry of Education and Research (BMBF)

Speaker: Prof. Dr. Markus Otto, Department of Neurology

Keywords: FTLD | Aphasia | Neuropsychology | dementia | biobanking

Frontotemporal lobar degeneration (FTLD) covers a whole spectrum of neurodegenerative disorders which principally affect the frontal and temporal lobes of the brain. Formerly, this group of diseases was referred to as Pick's disease, but there have been frequent changes to the name and the classification of frontotemporal lobar degeneration because it has been a subject of consistent and strong debate.

Currently, the following disorders are grouped together under the overall title of FTLD: (1) frontotemporal dementia (FTD) as behavioural variant; (2) primary nonfluent aphasia (PNFA); (3) semantic dementia (SD) as language variants; (4) amyotrophic lateral sclerosis with frontotemporal dementia (ALS+FTD); (5) corticobasal syndrome (CBS); and (6) progressive supranuclear palsy (PSP).

As well as the two principal groups of symptoms (changes in behavior and difficulties with speech), various extra-pyramidal motor symptoms may also become apparent, especially in the case of corticobasal syndrome and progressive supranuclear palsy.

There are very few studies regarding the frequency of these disorders, with estimates ranging from three patients per 100,000 of the population via 15 per 100,000 up to over 40 per 100,000. What is beyond doubt, however, is that the group of illnesses described under frontotemporal lobar degeneration represents the second most frequent dementia in patients under 65 years of age.

In terms of etiology, there has been considerable progress in recent years, with neuropathology successfully identifying tau aggregates as well as TDP43 and FUS inclusions as contributing factors. Meanwhile, genetics has identified several genes which are risk factors. Among clinical practitioners, however, even symptomatic treatment of FTLD illnesses is controversial. One of this consortium's central goals is to develop and evaluate parameters which will help clinicians to diagnose FTLD at an early stage and follow its progression, with the overall aim of developing effective objective targets for therapeutic strategies.

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Selected Publications:

- *Frisch S, Dukart J, Vogt B, Horstmann A, Becker G, Villringer A, Barthel H, Sabri O, Müller K, Schroeter ML. Dissociating memory networks in early Alzheimer's disease and frontotemporal lobar degeneration - a combined study of hypometabolism and atrophy. PLoS One. 2013;8(2):e55251.*
- *Otto M, Bowser R, Turner M, Berry J, Brettschneider J, Connor J, et al. (2012): Roadmap and standard operating procedures for biobanking and discovery of neurochemical markers in ALS. Amyotroph Lateral Scler;13:1-10.*
- *Otto M, Ludolph AC, Landwehrmeyer B, Förstl H, Diehl-Schmid J, Neumann M, Kretzschmar HA, Schroeter M, Kornhuber J, Danek A; FTLD consortium. [German consortium for frontotemporal lobar degeneration]. Nervenarzt. 2011;82(8):1002-5.*



Kick-off meeting of the MND-NET consortium in May 2013 at the Reisensburg, Günzburg.

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Molecular Mechanisms of Aging and Age-associated Diseases

Rare Neurodegenerative Diseases

MND-NET – the German ALS Network

Funded by the German Federal Ministry of Education and Research (BMBF)

Speaker: Prof. Dr. Albert C. Ludolph, Department of Neurology

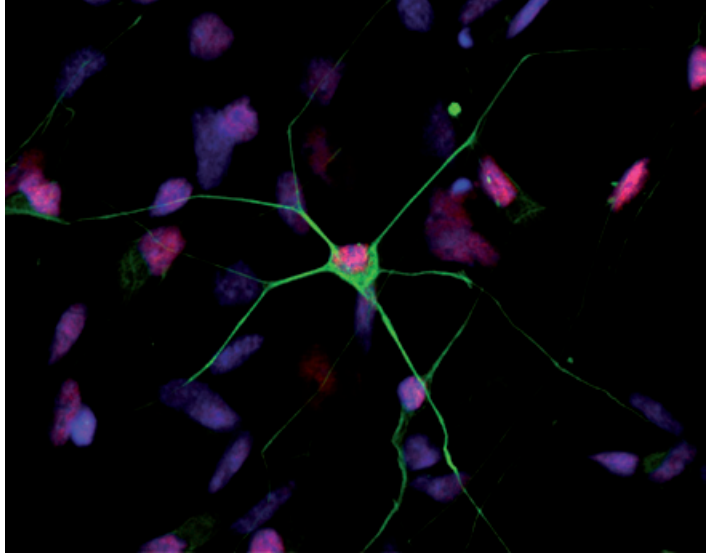
Keywords: ALS | motoneuron disease | biobank | patient registry

The disease course of ALS and other motoneuron diseases (MND) as well as the insufficient therapeutic options and numerous open questions regarding symptomatic, nutritive and psychosocial care for MND patients still require intensive investigations in large, meaningful and well-characterized study populations. In addition, patient registries necessary for efficient conduction of clinical trials and rapid evaluation of novel therapies are lacking. Furthermore, biosample collections established and based on standard operating procedures are urgently needed for the development of biomarkers and studies on molecular disease mechanisms.

The MND-NET is the clinical and scientific network of German motoneuron disease centers initiated and coordinated by the Department of Neurology of Ulm University. Our goal is to meet the above described needs and to improve patient care as well as the basis for clinical and basic research on this devastating group of diseases. The MND-NET comprises all large motoneuron disease centers across Germany and provides a valuable infrastructure for the improvement of motoneuron patient care and the advancement of motoneuron disease research.

Selected Publications:

- *Prause J, Goswami A, Katona I, Roos A, Schnizler M, Bushuven E, Dreier A, Buchkremer S, Johann S, Beyer C, Deschauer M, Troost D, Weis J. Altered localization, abnormal modification and loss of function of Sigma receptor-1 in amyotrophic lateral sclerosis. Hum Mol Genet. 2013;15;22:1581-600.*
- *Weishaupt JH, Waibel S, Birve A, Volk AE, Mayer B, Meyer T, Ludolph AC, Andersen PM. A novel optineurin truncating mutation and three glaucoma-associated missense variants in patients with familial amyotrophic lateral sclerosis in Germany. Neurobiol Aging. 2013;34(5):1516.e9-15.*
- *Dupuis L, Dengler R, Heneka MT, Meyer T, Zierz S, Kassubek J, Fischer W, Steiner F, Lindauer E, Otto M, Dreyhaupt J, Grehl T, Hermann A, Winkler AS, Bogdahn U, Benecke R, Schrank B, Wessig C, Grosskreutz J, Ludolph AC; GERP ALS Study Group. A randomized, double blind, placebo-controlled trial of pioglitazone in combination with riluzole in amyotrophic lateral sclerosis. PLoS One. 2012;7(6):e37885.*



A human motoneuron (in green) generated from a patient-derived pluripotent stem cell. The cell nucleus is shown in blue, and TDP-43, a RNA-binding protein dysfunctional in sporadic and familial ALS, is shown in red.

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Molecular Mechanisms of Aging and Age-associated Diseases

Rare Neurodegenerative Diseases

Helmholtz Virtual Institute: RNA Dysmetabolism in Amytrophic Lateral Sclerosis and Frontotemporal Dementia

Funded by the Helmholtz Association

Speaker of the University partner: Prof. Dr. Albert C. Ludolph, Department of Neurology

Keywords: Amyotrophic Lateral Sclerosis | Frontotemporal Dementia | RNA metabolism

The Helmholtz Virtual-Institute “RNA Dysmetabolism in Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Dementia (FTD)” was founded in January 2013 and is an international research center embedded in the German Center of Neurodegenerative Diseases (DZNE). The DZNE has the overall goal of understanding the cause and risk factors of neurodegenerative diseases with the potential of developing new therapeutic strategies. The Virtual Institute investigates the pathomechanisms of newly identified mutations causative for ALS and FTD involved in RNA metabolism. To this end, research groups from the DZNE located in Dresden (Prof. G. Kempermann; Dr. A. Hermann; Prof. A. Storch), Munich (Prof. Ch. Haass) and Tübingen (Prof. P. Kahle; Prof. M. Neumann) collaborate with research groups at Ulm University (Prof. T. Böckers; Prof. Ludolph; Prof. Weishaupt; Dr. A. Witting; Dr. P. Weydt; Dr. K. Lindenberg; Dr. S. Putz; Dr. S. Liebau) and associated partners at the INSERM (Prof. L. Dupuis, Prof. F. René; Prof. J.P. Loeffler, University of Strasbourg, France) and Sweden (Prof. P. Andersen, Umeå University) in order to combine basic research facilities, clinical expertise, and access to biological samples.

Selected Publications:

- *Eschbach, J., Schwalenstocker, B., Soyal, S.M., Bayer, H., Wiesner, D., Akimoto, C., Nilsson, A.C., Birve, A., Meyer, T., Dupuis, L., Danzer, K.M., Andersen, P.M., Witting, A., Ludolph, A.C., Patsch, W., Weydt, P. (2013) PGC-1alpha is a male-specific disease modifier of human and experimental amyotrophic lateral sclerosis. Hum Mol Genet, 22, 3477-3484.*
- *Rona-Voros, K., Eschbach, J., Vernay, A., Wiesner, D., Schwalenstocker, B., Geniquet, P., Mousson De Camaret, B., Echaniz-Laguna, A., Loeffler, J.P., Ludolph, A.C., Weydt, P., Dupuis, L. (2013) Full-length PGC-1alpha salvages the phenotype of a mouse model of human neuropathy through mitochondrial proliferation. Hum Mol Genet, 22, 5096-5106.*
- *Freischmidt, A., Müller, K., Zondler, L., Weydt, P., Volk, A.E., Božič, A.L., Walter, M., Bonin, M., Mayer, B., von Arnim, C., Otto, M., Dieterich, C., Holzmann, K., Andersen, P.M., Ludolph, A.C., Danzer, K.M., Weishaupt, J.H. (2014) Serum microRNAs in genetic amyotrophic lateral sclerosis patients and pre-manifest mutation carriers. Brain, in press.*



The team of the specialized ALS outpatient clinic and study center in Ulm.

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Molecular Mechanisms of Aging and Age-associated Diseases

Rare Neurodegenerative Diseases

Charcot Foundation and ALS Research Center

Funded by the Charcot Foundation

Speakers: Prof. Dr. Albert C. Ludolph and Prof. Dr. Jochen Weishaupt, Department of Neurology

Keywords: ALS | motoneuron disease | neurogenetics | epigenetics | ALS epidemiology

The Charcot Foundation has existed since 1999 and promotes research on patient care, molecular mechanisms of pathogenesis, and novel therapies with regard to ALS and other neurodegenerative diseases. It represents the umbrella organization supporting the Center for ALS Research, which bundles several different ALS research activities. Among these activities is the Swabian ALS registry, one of the largest epidemiological ALS registries, which provides information about the incidence as well as environmental and other factors causing ALS. Furthermore, a professorship for neurodegeneration has been implemented and is financed by the Charcot Foundation to elucidate the cell biological basis of ALS and to identify novel therapeutic target molecules. This also includes the application of high-throughput sequencing techniques to discover so far unknown genetic causes for familial ALS cases.

An additional field of research is the development of biomarkers for a better diagnosis and evaluation of therapeutic trials in ALS.

Selected Publications:

- *Hübers A, Marroquin N, Schmoll B, Vielhaber S, Just M, Mayer B, Högel J, Dorst J, Mertens T, Just W, Aulitzky A, Wais V, Ludolph AC, Kubisch C, Weishaupt JH, Volk AE. Polymerase chain reaction and Southern blot-based analysis of the C9orf72 hexanucleotide repeat in different motor neuron diseases. Neurobiol Aging 2014; 35(5): 1214.e1-6.*
- *Freischmidt A, Muller K, Ludolph AC, Weishaupt JH. Systemic dysregulation of TDP-43 binding microRNAs in amyotrophic lateral sclerosis. Acta Neuropathol Commun 2013; 1: 42.*
- *Weishaupt JH, Waibel S, Birve A, Volk AE, Mayer B, Meyer T, Ludolph AC, Andersen PM. A novel optineurin truncating mutation and three glaucoma-associated missense variants in patients with familial amyotrophic lateral sclerosis in Germany. Neurobiol Aging 2013; 34: 1516 e1519-1515.*



Molecular Mechanisms of Aging and Age-associated Diseases

Rare Neurodegenerative Diseases

CHDI (Cure Huntington's Disease Initiative) – USA/ (EHDN) European Huntington's Disease Network

Funded by the High Q Foundation

Speaker: Prof. Dr. G. Bernhard Landwehrmeyer, Department of Neurology

Keywords: Databanking | Huntington's Disease | international network | interventional studies | natural history

The European Huntington's Disease Network (EHDN) is dedicated to Huntington's Disease (HD), an inherited neurodegenerative disorder. EHDN provides a platform for professionals and people affected by HD, and for their relatives, and is sponsored by a not-for-profit foundation, CHDI Inc. (www.chdifoundation.org). EHDN's Executive Committee is chaired by Prof. Dr. G. B. Landwehrmeyer. EHDN includes 157 sites in 20 European countries that take part in a natural history study, REGISTRY. Its scientific planning committee and clinical trial task force as well as 21 working groups aim to facilitate research activities and clinical trial design.

Recently, the transition has begun from REGISTRY to Enroll-HD, a global observational study with the aim of enrolling 20-30,000 participants worldwide. An example of its goals is to correlate clinical characteristics with genetic factors and biomarkers and to expedite the identification and recruitment of participants for future clinical trials. Enroll-HD is open to recruiting participants at all stages of HD and gene negative family members, carers and control participants from North and South America, Australasia and Europe.

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Selected Publications:

- *HORIZON Investigators of the Huntington Study Group and European Huntington's Disease Network. A randomized, double-blind, placebo-controlled study of latrepirdine in patients with mild to moderate Huntington disease. JAMA Neurol. 2013;70(1):25-33. doi: 10.1001/2013.*
- *Sprengelmeyer R, Orth M, Müller HP, Wolf RC, Grön G, Depping MS, Kassubek J, Justo D, Rees EM, Haider S, Cole JH, Hobbs NZ, Roos RA, Dürr A, Tabrizi SJ, Süssmuth SD, Landwehrmeyer GB. The neuroanatomy of subthreshold depressive symptoms in Huntington's disease: a combined diffusion tensor imaging (DTI) and voxel-based morphometry (VBM) study. Psychol Med. 2013 Oct 7:1-12.*
- *Observing Huntington's disease: the European Huntington's Disease Network's REGISTRY. Orth M; the European Huntington's Disease Network J Neurol Neurosurg Psychiatry. 2011;82(12):1409-12.*

Molecular Mechanisms of Aging and Age-associated Diseases

Cardiometabolic Diseases (Diabetes and Obesity)

Consortium „Adolescents with Extreme Obesity“ within the Competence Network Obesity (CNO)



Funded by the German Federal Ministry of Education and Research (BMBF)

Speaker: Prof. Dr. Martin Wabitsch, MD, PhD, Department of Pediatrics and Adolescent Medicine

Keywords: adolescents with extreme obesity, body weight regulation, bariatric surgery

Extremely obese adolescents are at a strongly elevated risk of early death, somatic comorbidities, psychiatric disorders, and social isolation, including unemployment, due to both functional impairment and stigmatization. Despite the dire implications of extreme obesity in adolescents and the frequently overt (e.g. orthopedic disorders) and non-overt (e.g. hypertension) comorbidity, these adolescents are difficult to reach and treat in medical terms. Thus, only a small percentage actively seeks treatment. The underlying reasons are poorly understood and may presumably be attributed to the young age, a predominantly low educational and socioeconomic status, as well as to functional impairment due to inactivity and psychiatric comorbidity. Unsuccessful attempts to lose weight on their own and/or within the medical system may have led to frustration with respect to their behavior in seeking treatment.

In acknowledgement of this, we have developed the “Medical and psychosocial implications of extreme obesity in adolescents - acceptance and effects of structured care study,” which is known by its abbreviated title as: “Youth with Extreme obesity Study (YES).” YES aims at improving the medical care and social support structures for this so far widely ignored patient group.

We focus on the identification of these subjects (baseline examination) and their acceptance of diagnostic and subsequent treatment procedures. In a randomized controlled trial we investigate the effectiveness of a low key group intervention by not focusing on weight loss but by aiming at the provision of obesity-related information, alleviation of social isolation, school and vocational integration, and improvement of self-esteem in comparison to a control group treated in a conventional way by focusing on weight loss. Interested individuals who fulfill current recommended criteria for weight loss surgery are provided with a structured preparation and follow-up programs. All subjects are subsequently monitored within a long-term observational study to elucidate the medical and psychosocial outcome. Results of this study will improve the medical care and social support structures for youths with extreme obesity in Germany.

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Selected Publications:

- *M. Wabitsch, A. Moss, K. Kromeyer-Hauschild. Unexpected plateauing of childhood obesity rates in developed countries. BMC Med 12: 17 (2014).*
- *B.S. Lennerz, M. Wabitsch, H. Lippert, S. Wolff, C. Knoll, R. Weiner, T. Manger, W. Kiess,and C. Stroh. Bariatric surgery in adolescents and young adults-safety and effectiveness in a cohort of 345 patients. Int J Obes (Lond) 38(3):334-40 (2014).*
- *M. Wabitsch, A. Moss, T. Reinehr, S. Wiegand, W. Kiess, A. Scherag, R. Holl, R. Holle, and J. Hebebrand. Medical and psychosocial implications of adolescent extreme obesity -- acceptance and effects of structured care short: Youth with Extreme Obesity Study (YES). BMC Public Health. 13(1):789 (2013).*

Project registration numbers:

www.clinicaltrials.gov:
NCT01625325, NCT01703273, NCT02062164, NCT01662271, NCT01632098.
www.germanctr.de:
DRKS00004172, DRKS00004195, DRKS00004196, DRKS00004198, DRKS00004197.



Children in a *Healthy Boat* classroom

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Molecular Mechanisms of Aging and Age-associated Diseases

Cardiometabolic Diseases (Diabetes and Obesity)

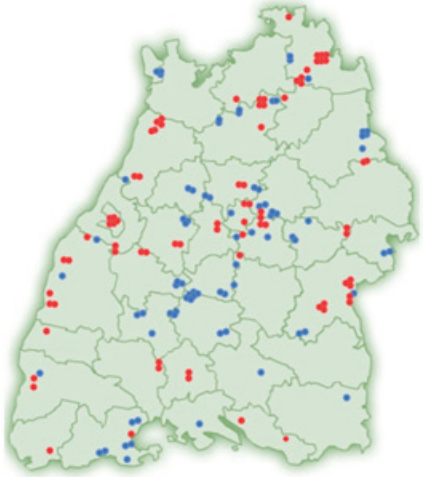
Join the Healthy Boat – Program for Health Promotion in Primary Schools

Funded by Baden-Württemberg Foundation

Speaker: Prof. Dr. Dr. h.c. Jürgen M. Steinacker, Department of Internal Medicine II

Keywords: Health promotion | children | life style | school-based | physical activity

Primary school classes taking part in the evaluation of Join the Healthy Boat (Baden-Württemberg Study)



red: intervention classes
blue: control classes

The statewide program, *Join the Healthy Boat,* promotes an active and healthy lifestyle for primary school children by offering healthy lifestyle choices in order to increase their physical, mental and emotional abilities. Based on the results of the URMEL-ICE Intervention trial, this program was started in 2009 in Baden-Württemberg. It has been developed, implemented and evaluated by a research team at Ulm University together with experienced teachers and is integrated into the school curriculum. So far, more than 2,000 primary school teachers have been trained and this corresponds to approximately 50,000 children.

Evaluation was performed in a randomized cohort study within a control group of 1,904 primary school children in 157 classes in Baden-Württemberg over a three-year period. The study showed positive intervention effects on body composition (waist circumference and skin folds), endurance (six minute run), quality of life and cost effectiveness. During the follow-up it was also shown that weight gain was associated with low physical activity, lack of active transport and lack of a regular breakfast. Waist-to-height was more predictive than BMI for the negative effects of obesity on quality of life and illness.

Selected Publications:

- *Drenowatz C, Kobel S, Kettner S, Kesztyüs D, Wirt T, Dreyhaupt J, Steinacker JM (2013): Correlates of weight gain in German children attending elementary school. Preventive Medicine, 57(4): 310-314.*
- *Kesztyüs D, Wirt T, Kobel S, Schreiber A, Kettner S, Dreyhaupt J, Kilian R, Steinacker JM (2013): Is central obesity associated with poorer health and health-related quality of life in primary school children? Cross-sectional results from the Baden-Württemberg Study. BMC Public Health, 13: 260.*
- *Kettner S, Kobel S, Fischbach N, Drenowatz C, Dreyhaupt J, Wirt T, Koch B, Steinacker JM (2013): Objectively determined physical activity levels of primary school children in south-west Germany. BMC Public Health, 13: 895.*



Executive Committee of the CRC1149:
(from left to right) Prof. Dr. Anita Ignatius (Coordinator);
Prof. Dr. Florian Gebhard (Speaker); and Prof. Dr. Markus Huber-Lang (Coordinator).

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Trauma Research (physical and psychic)/Musculoskeletal Research

Collaborative Research Center CRC1149

Funded by the German Research Foundation (DFG)

Speaker: Prof. Dr. Florian Gebhard, Department of Orthopedic Trauma, Hand, Plastic, and Reconstruction Surgery
Coordinators: Prof. Dr. Markus Huber-Lang, Dept. of Orthopedic Trauma, Hand, Plastic, and Reconstruction Surgery
Prof. Dr. Anita Ignatius, Institute of Orthopedic Research and Biomechanics

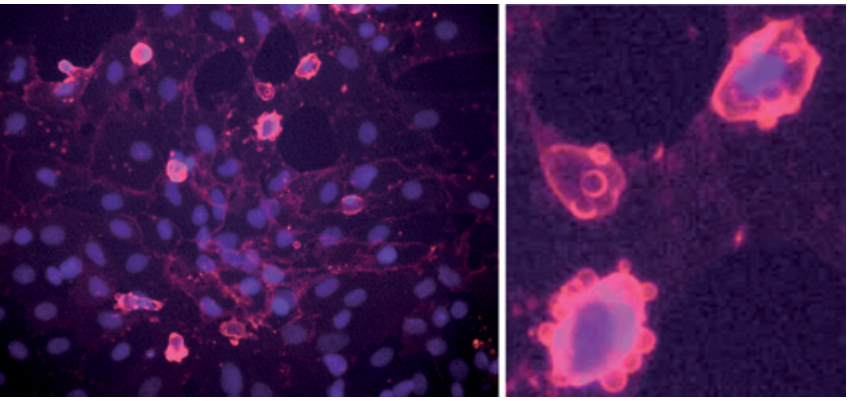
Keywords: Trauma | Disturbance Factors | Regeneration | Inflammation

Trauma affects a vast number of people worldwide at any time from birth to death. The trauma-triggered danger response induces potent regeneration and healing processes. However, significant complications, e.g. systemic inflammation and organ dysfunction, may develop post trauma, particularly in the presence of disturbance factors. The underlying pathophysiological mechanisms are complex and so far poorly understood. Focusing on common injury patterns, major disturbance factors, and regenerative mechanisms, this CRC initiative aims to provide a profound pathomechanistic understanding of the trauma response for transfer into effective therapeutic strategies.

The projects aim to elucidate:
(A) the acute cellular and molecular danger response after trauma;
(B) the perturbation of the posttraumatic response by relevant co-morbidities and substance abuse in regard to healing processes;
(C) the regenerative mechanisms, focusing on the role of inflammatory mediators and stem cells to modulate healing after severe trauma.
The close interaction of basic, translational and clinical research realized in this CRC will substantially contribute to a better understanding of trauma pathophysiology under “real-life” conditions, and to an improved clinical management for trauma patients.

Selected Publications:

- *Recknagel S et al (2013): Conversion from external fixator to intramedullary nail causes a second hit and impairs fracture healing in a severe trauma model. J Orthop Res, 31:465-471.*
- *Claes L et al. (2012): Fracture healing under healthy and inflammatory condition. Nat Rev Rheumatol, 8:133-143.*
- *Kanse SM et al. (2012): Factor VII-activating protease is activated in multiple trauma patients and generates anaphylatoxin C5a. J Immunol, 188:2858-2865.*



Enhanced programmed cell death (apoptosis) rate of lung epithelial cells after severe tissue trauma. The depicted cellular blebbing of lung epithelium represents an early sign of apoptosis.

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Trauma Research (physical and psychic)/Musculoskeletal Research

KFO 200 – Inflammatory Response following Musculo-Skeletal Trauma

Funded by the German Research Foundation (DFG)

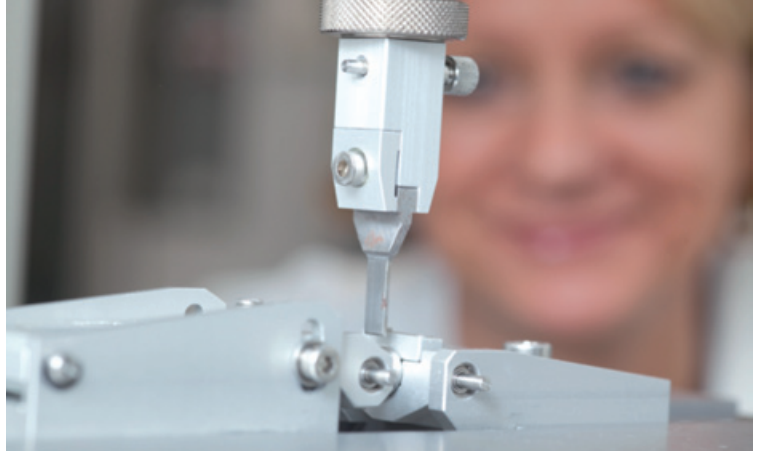
Speaker: Prof. Dr. Florian Gebhard · Leader: Prof. Dr. Markus Huber-Lang,
Department of Orthopedic Trauma, Hand, Plastic, and Reconstruction Surgery

Keywords: Complement | damage response | inflammation | lung injury | Trauma

Musculoskeletal injuries represent a lifetime danger for any human being and often result in severe acute and chronic disorders. Despite advances in trauma management and a better understanding of the underlying complex pathophysiology, the uncontrolled inflammatory response post injury remains a scientific and clinical challenge. Therefore, the KFO 200 investigates the danger and inflammatory response early after trauma. Based on various tissue trauma models and translational in trauma patients, research is mainly focused on the lungs as the “engine” of the inflammatory reaction, and on bone and cartilage tissues with their so far rather unrecognized immune potential. On a molecular level, the role of the “serine protease system” (complement-coagulation cascade) as the central fluid phase innate defense system is defined in trauma. Furthermore, to extend the concept of injury pattern- and time-adapted surgical “tissue damage control,” the KFO 200 aims to monitor more precisely the immune response in order to develop an innovative and highly specific immune control to improve molecular, cellular and organ function early after trauma, and thereby the outcome for the patient.

Selected Publications:

- *Unnewehr H, Rittirsch D, Sarma JV, Zetoune F, Flierl MA, Perl M, Denk S, Weiss M, Schneider ME, Monk PN, Neff T, Mihlan M, Barth H, Gebhard F, Ward PA, Huber-Lang M. Changes and regulation of the C5a receptor on neutrophils during septic shock in humans. J Immunol. 2013 Apr 15;190(8):4215-25.*
- *Gröger M, Scheuerle A, Wagner F, Simon F, Matallo J, McCook O, Seifritz A, Stahl B, Wachter U, Vogt JA, Asfar P, Matejovic M, Möller P, Lampl L, Bracht H, Calzia E, Georgieff M, Radermacher P, Stahl W. Effects of pretreatment hypothermia during resuscitated porcine hemorrhagic shock. Crit Care Med. 2013 Jul;41(7):e105-17.*
- *Recknagel S, Bindl R, Wehner T, Göckelmann M, Wehrle E, Gebhard F, Huber-Lang M, Claes L, Ignatius A. Conversion from external fixator to intramedullary nail causes a second hit and impairs fracture healing in a severe trauma model. J Orthop Res. 2013 Mar;31(3):465-71.*



Biomechanical testing of a bone specimen in a materials testing machine.

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Trauma Research (physical and psychic)/Musculoskeletal Research

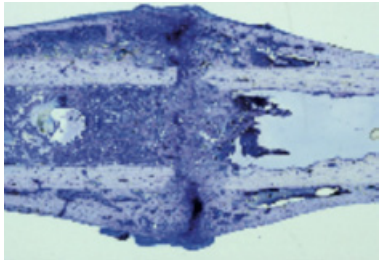
FOR 793 – Mechanisms of Fracture Healing and Bone Regeneration in Osteoporotic Bone

Funded by the German Research Foundation (DFG)

Speakers: Prof. Dr. Michael Amling, University Medical Center Hamburg-Eppendorf and Prof. Dr. Anita Ignatius, Institute of Orthopedic Research and Biomechanics

Keywords: Osteoporosis | bone | fracture healing | wnt signaling in bone

Osteoporosis predominantly affects postmenopausal women and is characterized by an imbalance between bone formation and resorption. The resulting bone loss is associated with fragility fractures, which frequently involve the spine and metaphyseal bone at the hip and wrist. Osteoporotic fractures are often associated with complications that lead to disability, increased mortality and socioeconomic burden. Complications are caused by poor primary stability of the fracture fixation in the fragile bone, which results in unfavorable mechanical healing conditions. Furthermore, the osteoporotic bone itself possesses reduced healing capacity. The underlying pathomechanisms are under extensive research with the aim of developing effective treatments to improve bone healing in osteoporotic patients. The research unit includes groups from the universities of Hamburg (Prof. M. Amling), Würzburg (Prof. F. Jakob) and Munich (Prof. W. Mutschler, Prof. E. Wolf). We are particularly interested in the role of Wnt/ß-catenin and estrogen receptor signaling pathways in bone regeneration. Further projects deal with the central regulation of bone healing or with the dysfunction of stem cells in osteoporotic bone.



Histological picture of newly formed bone near a fracture.

Selected Publications:

- *Heilmann A, Schinke T, Bindl R, Wehner T, Rapp A, Haffner-Luntzer M, Liedert A, Amling M, Ignatius A (2013): Systemic treatment with the sphingosine-1-phosphate analog FTY720 does not improve fracture healing in mice. Journal of Orthopedic Research, 31:1845-1850.*
- *Heilmann A, Schinke T, Bindl R, Wehner T, Rapp A, Haffner-Luntzer M, Nemitz C, Liedert A, Amling M, Ignatius A (2013): The Wnt Serpentine Receptor Frizzled-9 Regulates New Bone Formation in Fracture Healing. PLoS One, 8:e84232.*
- *Claes L, Recknagel S, Ignatius A (2012): Fracture healing under healthy and inflammatory conditions. Nature Review Rheumatology, 8:133-143.*



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Trauma Research (physical and psychic)/Musculoskeletal Research

Collaborative Project CANMANAGE: Case Management in Child Abuse and Neglect

Funded by the German Federal Ministry of Education and Research (BMBF)

Speaker: Prof. Dr. Dipl.-Psych. Lutz Goldbeck, Department of Child and Adolescent Psychiatry/Psychotherapy

Keywords: Case management | child abuse and neglect | evidence-based interventions | trauma-focused interventions.

Implementation of Managed Mental Healthcare for Children and Adolescents after Abuse and Neglect

Victims of child abuse and neglect (CAN) are at risk of developing chronic mental disorders. Although there are evidence-based treatments for this section of the population, the implementation, dissemination and utilization of these treatments are still insufficient. The consortium CANMANAGE has the primary objective of pursuing the improvement of mental healthcare for children and adolescents exposed to child abuse and neglect (CAN). At five German study sites, regional networks of care have been established and expanded. Children and adolescents between four and 17 years of age with a history of CAN are identified in cooperating institutions of the child welfare system or in the clinics of the study sites. They are asked to participate in a comprehensive psychological assessment. Those with unmet needs for treatment, together with their caregivers, receive recommendations and support to access the appropriate evidence-based treatments. Multiple outcomes are evaluated during regular follow-up assessments. Three projects have been implemented: 1. a randomized controlled trial of a case-management intervention; 2. resilience after CAN; and 3. migration, culture and CAN.

Selected Publications:

- *Domhardt, M., Fegert, J.M., Goldbeck, L. (in press). Resilience of Survivors of Child Sexual Abuse: A Systematic Review of the Literature. Trauma, Violence, & Abuse.*
- *Münzer, A., Fegert, J.M., Goldbeck, L. (in press). Please tell! Barriers of disclosing sexual victimization and subsequent social support perceived by children and adolescents. Journal of Interpersonal Violence.*
- *Münzer, A., Fegert. J.M., Goldbeck, L. (2014) Traumaanamnese und posttraumatische Stresssymptomatik in einer kinder- und jugendpsychiatrischen Inanspruchnahmepopulation. [Trauma history and posttraumatic stress symptoms among children and adolescents attending a mental health service]. Psychiatr Prax. 2014 Mar 18. [Epub ahead of print]*

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Trauma Research (physical and psychic)/Musculoskeletal Research

Collaborative Project TRANS-GEN: My Childhood – Your Childhood

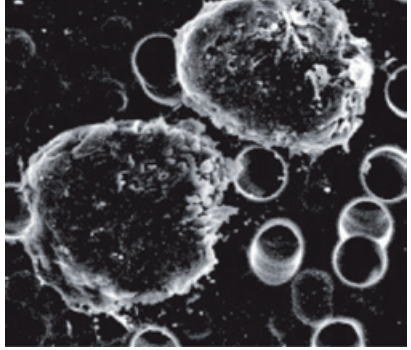
Funded by the German Federal Ministry of Education and Research (BMBF)

Speaker: Prof. Dr. Jörg M. Fegert, Department of Child and Adolescent Psychiatry/Psychotherapy

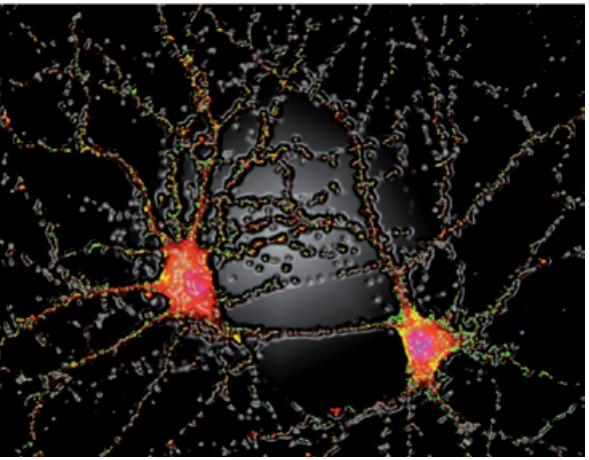
Keywords: Childhood maltreatment | resilience | transgenerational cycle

"TRANSGEN: Meine Kindheit – Deine Kindheit" is funded by the Federal Ministry of Education and Research (BMBF) and investigates mothers and their infants during the first year of life. Mothers with adverse experiences in their own childhood are at increased risk of maltreating their offspring, but the majority of them do not continue this "transgenerational cycle of maltreatment." The underlying dynamic process promoting the maintenance of a child's mental health in the face of severe adversity during the mother's lifetime is called resilience.
We recruit mothers who have given birth in the maternity clinic of the University Hospital Ulm. They are followed up after three and twelve months. We also investigate the psychological development of infants at twelve months and identify psychological, biological and social factors which especially promote resilience during the first year of the developing mother-infant dyad. A parallel animal model allows a deeper understanding of the biological underpinnings of resilience in a transgenerational context. Empirical data on this issue would enable professionals and social systems to target and offer much more effectively adequate services to mothers and children at risk.





Migration of inflammatory cells (neutrophils) through micropores towards danger signals, released after trauma and visualized by scanning electron microscopy.
Research group of S. Paschke.



The effects of traumatic brain injury on the neuronal cross-talk are investigated by the research groups of T. Böckers and M. Huber-Lang.

Trauma Research (physical and psychic)/Musculoskeletal Research

Innnovation Fund Medicine: Trauma

Funded by the State of Baden-Württemberg

Speakers: Prof. Dr. Markus Huber-Lang, Department of Orthopedic Trauma-, Hand-, Plastic-, and Reconstruction Surgery
Prof. Dr. Anita Ignatius, Institute of Orthopedic Research and Biomechanics

Keywords: Trauma | Danger Response | Regeneration | Immune-Modulation

The Research Center focuses on the danger response and regeneration after musculoskeletal trauma which is a topic of the highest scientific, clinical and socio-economic relevance. Any trauma results in local tissue damage that, depending on the extent of the trauma impact, may lead to severe morphological and functional defects. Furthermore, any severe trauma can trigger a systemic danger response of the whole body that involves not only primarily injured organs but also the development of remote organ injury. The systemic and local posttraumatic reactions are exceedingly complex and are so far not fully understood. Therefore, the research consortium of the Innovation Fund Medicine (*Perspektivförderung Trauma*) investigates the cellular and molecular mechanism of the posttraumatic danger response in clinically relevant models of tissue damage (traumatic brain injury, fracture, thorax-, soft-tissue-, and poly-trauma). In translational approaches, the danger response and regeneration processes are also elucidated in trauma patients on an organ, cellular and molecular level with the aim of developing improved therapeutic strategies for severely injured patients in order to improve the acute and long-term outcome and quality of life after trauma.

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Selected Publications:

- *Schmeisser MJ, Ey E, Wegener S, Bockmann J, Stempel AV, Kuebler A, Janssen AL, Udvardi PT, Shiban E, Spilker C, Balschun D, Skryabin BV, Dieck St, Smalla KH, Montag D, Leblond CS, Faure P, Torquet N, Le Sourd AM, Toro R, Grabrucker AM, Shoichet SA, Schmitz D, Kreutz MR, Bourgeron T, Gundelfinger ED, Boeckers TM. Autistic-like behaviours and hyperactivity in mice lacking ProSAP1/Shank2. Nature. 2012 Apr 29;486(7402):256-60.*
- *Paschke S, Weidner AF, Paust T, Marti O, Beil M, Ben-Chetrit E. Technical advance: Inhibition of neutrophil chemotaxis by colchicine is modulated through viscoelastic properties of subcellular compartments. J Leukoc Biol. 2013, Nov;94(5):1091-6.*
- *Ehrnthaller C, Huber-Lang M, Nilsson P, Bindl R, Redeker S, Recknagel S, Rapp A, Mollnes T, Amling M, Gebhard F, Ignatius A. Complement C3 and C5 deficiency affects fracture healing. PLoS One. 2013 Nov 18;8(11):e81341.*



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Trauma Research (physical and psychic)/Musculoskeletal Research

Competence Center Child Abuse and Neglect

Funded by the State of Baden-Württemberg

Speaker: Prof. Dr. Jörg M. Fegert, Department of Child and Adolescent Psychiatry/Psychotherapy

Keywords: Child abuse and neglect | competence center | basic and advanced training

Child abuse and neglect have attracted much public interest in recent years and have also entailed the development of new initiatives and research projects in this field. In the medical field especially, it is of utmost importance to raise awareness and to improve the treatment of those affected. General standards for diagnostic procedures are necessary and the training of physicians on the topic of child protection needs to be improved. To address these concerns, the Competence Center Child Abuse and Neglect (www.comcan.de) was founded in Ulm in 2013 in cooperation with the university hospitals in Heidelberg and Freiburg and is sponsored by the Baden-Württemberg Ministry of Science, Research and the Arts (MWK).The competences of the disciplines of child and adolescent psychiatry, pediatrics and forensic medicine have thus been brought together. The aim of the center is to improve the basic and advanced training of medical professionals in Baden-Württemberg on matters of child protection. One important step will be the establishment of a curriculum for medical students. Furthermore, research and translational activities are additional important aims of the new competence center.

Selected Publications:

- *Fegert JM, Jud A, Plener PL (2013) Kinderschutz und Betroffenenschutz in der Medizin. Nervenheilkunde 32: 834-841.*
- *Witt A, Rassenhofer M, Pillhofer M, Plener PL, Fegert JM (2013) Das Ausmaß von Kindesmissbrauch, -misshandlung und -vernachlässigung in Deutschland: eine Übersicht zu Definitionen, Prävalenz, Folgen, Risiko- und Resilienzfaktoren. Nervenheilkunde 32: 813-819.*



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Cross-sectional Centers

GSC 270 – International Graduate School in Molecular Medicine

Funded by the Excellence Initiative of the German federal and state governments

Speaker: Prof. Dr. Michael Kühl, Institute of Biochemistry and Molecular Biology

Keywords: Graduate School | Scientific excellence | Internationality | PhD | Double degree

Scientific excellence depends on excellently trained young researchers. The training of such researchers is the aim of the International Graduate School in Molecular Medicine Ulm founded in 2006. Today, as of October 2014, more than 300 PhD students are or have been members of the Graduate School and more than 90 students have successfully finished the program. The PhD training offered is organized in thematically focused Research Training Groups representing the research topics of the Medical Faculty: (i) Development, Aging and Regeneration, (ii) Signaling Networks in the Hematopoetic System and Oncology, (iii) Cardio-metabolic Disorders, and (iv) Host-Microbe Interaction. Each PhD student is supervised by a Thesis Advisory Committee consisting of the main supervisor, a scientist from another institute of Ulm University and an international external reviewer from academia or industry. Students are actively integrated into the scientific community by giving scientific talks and poster presentations at international meetings. In addition to curricular seminars and lectures, a large variety of optional activities, such as key competence seminars, is offered. Graduates can choose between the international degree of PhD or the German degree Dr. rer. nat. The Graduate School offers double degrees with either the University of Padua (Italy) or the BioCenter Oulu (Finland). The maintenance of our high standards is guaranteed through the accreditation of our PhD program, regular advice from our international Scientific Advisory Board and a yearly evaluation by the PhD students. The Graduate School is funded by the Excellence Initiative of the German federal and state governments and represents another endorsement of our high scientific and educational quality and profile.

Selected Publications:

- *Faber K, Bullinger L, Ragu C, Garding A, Mertens D, Miller C, Martin D, Walcher D, Döhner K, Döhner H, Claus R, Plass C, Sykes SM, Lane SW, Scholl C, Fröhling S (2013): CDX2-driven leukemogenesis involves KLF4 repression and deregulated PPARγ signaling. J Clin Invest. 123(1): 299-314.*
- *Wang J, Sun Q, Morita Y, Jiang H, Gross A, Lechel A, Hildner K, Guachalla LM, Gompf A, Hartmann D, Schambach A, Wuestefeld T, Dauch D, Schrezenmeier H, Hofmann WK, Nakauchi H, Ju Z, Kestler HA, Zender L, Rudolph KL (2012): A differentiation checkpoint limits hematopoietic stem cell self-renewal in response to DNA damage. Cell. 148(5): 1001-14.*
- *Schmeisser MJ, Ey E, Wegener S, Bockmann J, Stempel AV, Kuebler A, Janssen AL, Udvardi PT, Shiban E, Spilker C, Balschun D, Skryabin BV, Dieck St, Smalla KH, Montag D, Leblond CS, Faure P, Torquet N, Le Sourd AM, Toro R, Grabrucker AM, Shoichet SA, Schmitz D, Kreutz MR, Bourgeron T, Gundelfinger ED, Boeckers TM (2012): Autistic-like behaviours and hyperactivity in mice lacking ProSAP1/Shank2. Nature. 486(7402): 256-60.*



In search of the neural correlates of consciousness with the electroencephalogram.

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Additional Topics

PAK 270 – Neuro-Cognitive Mechanisms of Conscious and Unconscious Visual Perception

Funded by the German Research Foundation (DFG)

Speaker: Prof. Dr. Markus Kiefer, Department of Psychiatry and Psychotherapy III

Keywords: Cognitive neuroscience | consciousness | psychology | unconscious visual perception | visual awareness

For a long time, elucidating human consciousness has been a task restricted to philosophers. In recent years, however, investigators of the neurosciences and psychology have used approaches to explain and gain a better understanding of this state of mind. Our research network aims at solving the riddle of consciousness from a cognitive neuroscientific perspective. In eleven research projects, general mechanisms governing conscious and unconscious visual perception are identified, both at a functional behavioral and at a neural level. This research network investigates how conscious differs from unconscious visual processing and identifies the mechanisms responsible for the selection and integration of visual information that contributes to conscious visual perception. It determines how these selection and integration mechanisms are implemented in the brain and specifies through which neural structures attention modulates conscious and unconscious perception. More specifically, we propose that conscious visual perception depends on recurrent activation within the visual system that leads to a consolidation of representations and a subsequent encoding of these representations into prefrontal working memory circuits. To address these important questions of consciousness research, classical psychological behavioral measures as well as neurophysiological measures of brain activity (event-related potentials; functional magnetic resonance imaging) are applied.

Selected Publications:

- *Ulrich, M., Hoenig, K., Groen, G., & Kiefer M. (2013). Brain activation during masked and unmasked semantic priming: Commonalities and differences. Journal of Cognitive Neuroscience, 25, 2216-2229.*
- *Chen, Q., Weidner, R., Vossel, S., Weiss, P. H., & Fink, G. R. (2012). Neural mechanisms of attentional reorienting in three-dimensional space. The Journal of Neuroscience, 32(39), 13352–13362.*
- *Martens, U., Ansorge, U., & Kiefer , M. (2011). Controlling the unconscious: Attentional task sets modulate subliminal semantic and visuo-motor processes differentially. Psychological Science, 22, 282–291.*



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Additional Topics

Center of Excellence for Rare Diseases Baden-Württemberg

Funded by the State of Baden-Württemberg

Speaker: Prof. Dr. Dr.h.c. Frank Lehmann-Horn, Division of Neurophysiology

Keywords: stem cell therapy | collagen disorders | dentition difficilis| Duchenne dystrophy | rare disease

Nearly 5% of the German population suffers from a rare disorder. Because of this low prevalence, rare diseases remain unrecognized by resident physicians and there is a lack of information regarding diagnosis and treatment possibilities. In order to address this issue, centers for the study of rare diseases have been established at all five medical centers in Baden-Württemberg (Freiburg, Heidelberg, Mannheim, Tübingen and Ulm). Together they comprise the Center of Excellence for Rare Diseases Baden-Württemberg which has been established to create an integrative structure incorporating education, research and care. Research focuses on four main areas: 1. stell cell therapy in hereditary bone marrow diseases; 2. therapy of genetic disorders of skin and collagen, including scleroderma and vasculitis; 3. dental disorders, including dentitio difficilis; and 4. treatment strategies for Duchenne muscular dystrophy. In addition, the center is developing a database for expert profiles of rare diseases using webcrawler strategies which update automatically.

Selected Publications:

- *Pflugrad, A., Jurkat-Rott, K., Lehmann-Horn, F., & Bernauer, J. (2014). Towards the Automated Generation of Expert Profiles for Rare Diseases through Bibliometric Analysis. Studies in health technology and informatics, 198, 47.*
- *Schuetz C, Pannicke U, Jacobsen EM, Burggraf S, Albert MH, Hönig M, Niehues T, Feyen O, Ehl S, Debatin KM, Friedrich W, Schulz AS, Schwarz K (2013). Lesson from hypomorphic recombination-activating gene (RAG) mutations: Why asymptomatic siblings should also be tested. J Allergy Clin Immunol. 2013.*
- *Moinzadeh P, Aberer E, Ahmadi-Simab K, Blank N, Distler JH, Fierlbeck G, Genth E, Guenther C, Hein R, Henes J, Herich L, Herrgott I, Koetter I, Kreuter A, Krieg T, Kuhr K, Lorenz HM, Meier F, Melchers I, Mensing H, Mueller-Ladner U, Pfeiffer C, Riemekasten G, Sárdy M, Schmalzing M, Sunderkoetter C, Susok L, Tarner IH, Vaith P, Worm M, Wozel G, Zeidler G, Hunzelmann N; and all participating DNSS centers. Disease progression in systemic sclerosis-overlap syndrome is significantly different from limited and diffuse cutaneous systemic sclerosis. Ann Rheum Dis. 2014 Jan 3. doi: 10.1136/annrheumdis-2013-204487.*



The Center of Medicine and Society.

Additional Topics

Center of Medicine and Society

Funded by the State of Baden-Württemberg

Speaker: Prof. Dr. Heiner Fangerau, Institute of the History, Philosophy and Ethics of Medicine

Keywords: Interdisciplinarity | Networking | Prevention of Child Abuse | Research on Health Provision | Medical Humanities | Research Innovation

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In the field of biomedical sciences, responsible future-orientated research can only be realized in a dialogue with society and under the consideration of historical, theoretical and ethical basic principles of medical research and action. In this respect, the Center of Medicine and Society intends to offer an interdisciplinary and multiperspective approach. Sixty one scientists and researchers from all academic fields are engaged in the projects of the Center of Medicine and Society.

The duties of the Center of Medicine and Society are:

1. The establishment of research groups focused on central points of intersection between medicine and society.
2. Accomplishment of profiled events and symposia.
3. Crosslinking initiatives of Ulm University in medical research fields of societal relevance.
4. Crosslinking of research in medical care that includes the fields of health economics and economic science.

Between 2013 and 2014, the center was able to fund and organize funding for the following multidisciplinary symposia:

The mechanization of old age – ethical, legal, social and medical aspects of assisting systems for senior citizens in need of care (Summer School, July 2013, BMBF).

The Center of Medicine and Society was of significant importance in the coordination and organization of the following successfully funded projects:

- Preventive decisions: The interaction of science, politics and the public in the implementation of national prevention programs for children and adolescents (2013-2016, MWK).
- Child well-being as a boundary object? Description and analysis of basic terms in child care in order to establish a culture of transparency in debates about child abuse in pedagogical institutions (H. Fangerau (Speaker), U. Ziegenhain, R. Tippelt, W. Viehöver, D. Birnbacher (2013-2016, BMBF).
- Stress resilience in the transgenerational transmission of childhood maltreatment. J. Fegert (Coordinator), H. Gündel, I.-T. Kolassa (2013-2016, BMBF).
- Innovations in teaching medical students, “Medicine and medical ethics in computer games” (2013-2014, Deutscher Stifterverband, Baden-Württemberg Stiftung).

Selected Publications:

- *Fegert JM, Kölch M, Fangerau H (2012): “Die Beschneidung aus ärztlicher Sicht und aus Sicht des Gesetzgebers”, MMW – Fortschritte der Medizin 154 (19): 47-50.*
- *Henn K, Fangerau H, Fegert J (2012): “Verhaltenes Engagement in der Jugendhilfe: Betrifft Inklusion etwa nur das Schulwesen? Herausforderungen und Fragestellungen auf dem Weg zur Realisierung einer ‘großen Lösung’ Jugendhilfe”, Das Jugendamt - Zeitschrift für Jugendhilfe und Familienrecht 85 (10): 504-509.*
- *Fegert J, Fangerau H, Besier T, Ziegenhain U (2011): “Fehlerprävention in der Kinderpsychiatrie”, Psychotherapie und Sozialwissenschaft 13(2): 91-108.*



Promotion of Young Scientists

Promotion of Young Scientists

The promotion of young scientists is one of the most important tasks of the Medical Faculty and the University Medical Center. We offer a variety of compatible programs on different educational levels as described below in order to support and actively encourage our junior researchers.



International Graduate School
in Molecular Medicine Ulm
IGradU

Training of PhD Students

International Graduate School in Molecular Medicine Ulm (IGradU)

Speaker: Prof. Dr. Michael Kühl, Institute of Biochemistry and Molecular Biology; www.uni-ulm.de/mm

In February 2006, Ulm University founded the *International Graduate School in Molecular Medicine* Ulm with the intention of providing high-quality postgraduate training. The Graduate School has been supported by the Excellence Initiative of the German federal and state governments since 2007 and was positively reevaluated in 2012 for an additional five years. The goal of the *Graduate School* is to introduce doctoral candidates at Ulm University conducting research in the field of biomedicine to a structured postgraduate program. Today (as of August 2014), the *Graduate School* supervises around 192 natural science and 34 medical doctoral candidates. The *Graduate School* is directed by a board which in turn is advised by an international and scientific advisory committee. There are two structured training programs on offer: the *International PhD Program in Molecular Medicine* for doctoral candidates of the natural sciences; and the program *Experimental Medicine* for doctoral candidates of medicine.

The International PhD Program in Molecular Medicine

Speaker: Prof. Dr. Michael Kühl, Institute of Biochemistry and Molecular Biology; www.uni-ulm.de/mm

This English-language postgraduate course offers a three-year structured doctorate. The course was accredited in March 2009 and reaccredited in 2014. The admission regulations stipulate clear criteria for selection: above-average degrees (MSc, state exam); proof of proficiency in English; a presentation before members of the faculty; and individual interviews with supervisors and members of the examination board (PhD committee). During their postgraduate course, doctoral candidates are monitored by a *Thesis Advisory Committee* consisting of three supervisors. A recent development has been the possibility of including a fourth supervisor to allow the supervision of PhD students by members of the *Junior Faculty of IGradU*. Each student's coursework is calculated and accredited according to the *European Credit Transfer and Accumulation System* (ECTS). After having successfully defended their thesis, graduates opt to receive either the international academic title of PhD or the German academic title Dr. rer. nat. The academic title of PhD can be extended in line with the subject area of the doctorate (e.g. PhD in Neurosciences). The course is also open to graduates of Human Medicine. The opportunity for graduates in this field to obtain the academic title of Dr. rer. nat. or PhD is a unique feature of the Medical Faculty and the *Graduate School* at Ulm University. This aspect will continue to make Ulm more attractive in the future and to strengthen its importance on an international level.



Experimental Medicine

Speaker: Prof. Dr. Thomas Wirth, Institute of Physiological Chemistry;
www.uni-ulm.de/einrichtungen/mm/expmedizin.html

In 2005, in order to combat deficiencies in the supervision and quality of medical theses, the Medical Faculty implemented the structured training program *International PhD Program in Experimental Medicine*, which was subsequently adopted by the *Graduate School* in 2009. The requirement for entry is an above-average intermediate examination (part one of the national medical licensing exam). Doctoral candidates must interrupt their studies in medicine for nine months in order to concentrate fully on their experimental work. The Medical Faculty and *IGradU* support this program with up to 35 stipends yearly (€500 per month over ten months). Doctoral candidates submit reports on their research work in the program's seminars in addition to giving presentations of up-to-date scientific literature in a *Journal Club*.



Students at Huazhong University of Science and Technology (HUST) in Wuhan at the 7th Summer School held by IGradU, Ulm



At the Padua Retreat

Extracurricular activities

Extracurricular activities, such as mobility and gender programs, retreats, and interaction with industry, complete the portfolio. One further key area is to establish and develop international contacts. For this reason, the *Graduate School* has been running its *Summer School in Molecular Medicine* every year since 2007 by offering a range of regularly changing topics at one of ten leading Chinese universities: the Huazhong University of Science and Technology (HUST) in Wuhan. Following an external review by the DAAD in 2007, the *Summer School* series was granted support and now continues with the help of funds provided by the Excellence Initiative. This means of recruitment has proven to be very successful and several doctoral candidates with Chinese postgraduate scholarships are now engaged in research in the laboratories of the Medical Faculty. Furthermore, summer schools, workshops and symposia are being held jointly with the *Graduate School* of the Biocenter Oulu in Finland (e.g. a workshop on mouse genetics took place in 2009). As a result, a second joint bilateral postgraduate program has been set up with the Biocenter Oulu (double doctorate) where the kick-off meeting took place in September 2013 and another retreat will take place in Autenried in September 2014.

Already in 2010, a joint PhD program with the University of Padua in Italy was set up and the first doctoral candidate graduated from this program in December 2013. A close partnership with the University of North Carolina at Chapel Hill, USA, has also been developed. Joint retreats took place in Switzerland and in Asheville, North Carolina. In September 2013, the *Graduate School* established a further cooperation in China by setting up a scientific exchange program with the Medical School of Southeast University in Nanjing. The first Chinese students have already finished their practical work in the laboratories of Ulm University.

Further Graduate School Activities

The *Graduate School* also offers a broad spectrum of key competence events (biosafety, good scientific practice, bioethics, project management, patent law, writing scientific texts etc.) and mentoring programs (e.g. M4M; see www.uni-ulm.de/einrichtungen/zawiw/m4m.html). These are open to students from both programs as well as to members of the postgraduate program *GRK 1789 – CEMMA: Cellular and Molecular Mechanisms in Aging*.

Guest Professor and Guest Scientist Programs

Furthermore, the *International Graduate School in Molecular Medicine* has established two *Guest Professor and Guest Scientist Programs* that aim to strengthen and improve international cooperation, enhance the international character of the *Graduate School* and expand the teaching offered to our students.

The first program is funded with a grant amounting to €50,000 by the state of Baden-Württemberg and aims to bring renowned and top-class experts to Ulm. This program includes the founding of a Junior Research Group in Ulm. The Guest Professor is expected to visit Ulm several times during the program and to contribute to research and teaching at the *Graduate School*.

The second program is a *Guest Scientist/Guest Professor Program* that allows collaborating partners to visit Ulm for a period of between 10 and 14 days to strengthen their collaboration and work in the labs as well as holding talks and offering courses for our students.



Prof. Philip Wong, Baltimore, guest professor at the International Graduate School in Molecular Medicine Ulm.

Junior Faculty

Moreover, the *Junior Faculty (JF)* at *IGradU* is a newly established program for junior researchers working at either Ulm University or the University Medical Center Ulm. Junior researchers have obtained a PhD but have yet to attain a permanent faculty position. The overall aim of the *Junior Faculty* is to promote the careers of young scientists through active interaction with the university, the faculty boards, and society. Joining the *Junior Faculty* offers the following benefits:

- The opportunity to conduct PhD-supervision as a member of a TAC (Thesis Advisory Committee)
- The support of supervisors
- Opportunities to receive financial support for further and continuing education
- Mentoring (gender programs, dyadic mentoring, peer-to-peer mentoring).

In order to become a member of the *Junior Faculty*, either a grant or secured outside funding, (e.g. outside funding from BMF, DFG, EU-Programs, Programs of the Medical Faculty of Ulm University, *Margarethe von Wrangell*-habilitation program for women etc.) or two corresponding authorships are required. There are currently 15 postdocs at Ulm University that are members of the *Junior Faculty* and are supervised by one speaker. They meet on a quarterly basis, discuss their projects and plan a number of additional activities. Activities of the *Junior Faculty* range from continuing education courses, support for pedagogic workshops (e.g. “The Teaching Certificate of the State of Baden-Württemberg”), to participation in the annual science fairs and JF-meetings.



Promoting the Early Scientific Independence of Young Scientists (Postdocs)

Alongside those projects mentioned above, the Medical Faculty also offers two programs to promote early scientific independence:

Individual Grants Program

Through the Individual Grants Program, the Medical Faculty awards start-up funding on a yearly basis and in a competitive manner for approximately 20 research projects proposed by junior physicians and natural scientists up to a maximum of €35,000 per annum. After the initial funding over a period of two to three years, these projects will subsequently be financed by external funding agencies.

Rotation Positions (“*Gerok* positions”)

The aim of this funding is to allow junior clinicians with doctorates the freedom to conduct research over a period of one to two years without any clinical duties. The five “*Gerok* positions” are also awarded yearly and competitively in a manner similar to those distributed through the Individual Grants Program. One condition for funding is the full-time release of employees for this project.

Continuing Medical Education



Online Master's Program in Advanced Oncology: Study part-time – team up internationally!

Speaker: Dr. Uta Schmidt-Straßburger; www.masteroncology.de

The Medical Faculty of Ulm University has launched the international postgraduate, blended learning study program in *Advanced Oncology* aimed at clinical oncologists and scientists involved in the field of oncology. Founded by internationally renowned experts with leading cooperating partners, the study program prepares participants to face the growing worldwide demand for the harmonized health care of cancer patients. Successful completion of the program leads to an MSc degree and offers a relevant qualification for leading positions. The innovative curriculum includes modules such as interdisciplinary oncology, clinical research, advanced therapies and integrated concepts, management and business administration. The online lectures are completed by soft skill training and personal development coaching. This Master's program is not only taught but also requires the completion of a self-written Master's thesis.

The university's international study program was established with the financial support of the Ministry for Science, Research and Art of the State of Baden-Württemberg. By taking into consideration time and location, the program's structure has been designed to allow for a flexible approach to learning so that participants can successfully combine the demands of work, family and study at their place of residence.



Training and Education



Experiencing a real life operation.



A student practicing on an artificial arm dummy.

Aims

The central aims of the Faculty of Medicine at Ulm University are the continuous development of its curricula, the improvement of its learning approach and the evaluation of its study setting. The Dean's Office for study affairs is responsible for the organization of all aspects of medical education, for example, management of the curricula, counseling for students and teachers, and support for innovations in teaching. This routine and service section as well as project realization is integrated into a competent statewide network specializing in medical education. In this report, we would like to give some examples of the teaching projects realized in cooperation with the faculty's commission on medical education that have brought together academic faculties, student representatives and the university's administration.

The Medical Faculty of Ulm University offers courses of studies in Medicine, Dentistry and Molecular Medicine (Bachelor, Master, PhD). In the following we will summarize the main features of these courses of studies and those aspects specific to Ulm University.

med[at]ulm
mehr studium + mehr leben

Medicine

Our concept of teaching and learning: MED@Ulm

We developed MED@ULM as a modern concept of medical education within the regular framework of the German License Order. This explicit adoption of the German License Order as a common and widespread framework guarantees the highest possible degree of mobility for medical undergraduate students.

The specific strength of MED@ULM as a modern medical curriculum is based upon several factors:

Definition of a specific education profile
Similar to the well-known CanMeds model, we have defined an education profile for our students by placing the medical expert in the center and by arranging eight further fields of competence around and connected to this center (see illustration). Regular evaluation of our curriculum, together with regularly performed requests for proposals, serve as vehicles to continuously improve the aims and goals of the education profile.

Implementation of individual study tracks
Although more than 300 students start their studies in the Faculty of Medicine at Ulm every year, we are convinced that personal and specific study tracks promote individual medical careers for the best students more effectively than a completely uniform study course. Therefore, our students may, if they wish, make their choice and implement their individual study focus, whether in neurological science, heart and lung medicine, trauma research and trauma management, general medicine or in experimental medicine. It is thus our aim to promote the careers of future professionals.

Implementation of a highly evolved peer teacher program
Students are engaged as peer teachers and are taught how to teach their junior colleagues – this is possibly the most concise summary of a program that consists of a series of seminars and tutorials for students who are interested in supporting the teaching of experts. Peer teachers are involved in communication training, lab skills training, and bedside teaching in order to allow much more intensive training units than any one professor could guarantee without this valuable support.

Implementation of elective courses in the curricular framework
Besides the obligatory seminars and the regular lectures of our curriculum, more than 80 elective courses are currently offered that include laboratory work as well as all aspects of patient care and scientific research. From this comprehensive program each individual student chooses a minimum of 70 elective hours during his/her study course and this has resulted in many students voluntarily attending considerably more seminar units than is actually required.



Implementation of individual time slots for scientific work
In contrast to many other medical faculties we allow our students complete freedom when to start with their doctoral thesis. Each student has, at any given time, the possibility of choosing a six-month period to concentrate on the demands of the scientific work necessary for a doctoral thesis (see also program Experimental Medicine on page 63). After this period, students can return to their regular studies without losing any continuity in their personal study course.

Implementation of mosaic curricula for multi- and interdisciplinary subjects
Gender medicine, palliative care, and pain medicine are three examples of medical fields that have an above-average degree of multi- and interdisciplinarity. We decided to implement these highly important fields into our curriculum without increasing the study load for our students by devising a teaching and learning mosaic: From early phases of the study course up until graduation various experts teach different aspects of each respective subject that is embedded in their lectures and seminars. A synopsis of all aspects taught is reflected on the learning platform MOODLE and also, in part, in synopsis seminars at the end of the study course.

Skills Labs, Simulated and Standardized Patients in Medical Education

In our skills labs the student is given the possibility of learning and being trained in manual skills in a controlled learning environment. This training phase is of enormous significance especially for all procedures that may be painful or dangerous, or may have the potential to embarrass a patient, as in the case of urological or gynecological examinations, vessel punctures, drainages, endotracheal intubation, and the bandaging of injured limbs. Beyond the regular teaching units in the skills lab, the students are invited to deepen their training experience during the “open training hours” where peer teachers act as supervisors for their junior colleagues.

One of our skills labs, and also one of the best equipped, deals exclusively with emergency procedures. The range of the procedures trained here covers minor emergencies as well as highly complex emergency scenarios where the future physician is expected not only to handle injured, distressed or unconscious emergency patients but also to act as a responsible team leader and coordinator. This is one of the labs where simulated patients are treated to create true-to-life scenarios.

Since 2008, Ulm University has employed simulated patients (SP) in medical training. By employing SPs, the communicative and social skills of students can be optimized and this makes it possible to teach students useful ways to deal with patients even in difficult and stressful situations. The SPs are trained to act as patients suffering from various diseases and are given extensive training to be able to offer constructive feedback to students after each role play. SPs are used in various programs, for example, Emergency Room, which is a program in emergency medicine, and the inter-disciplinary program, *Communication in Difficult Situations in Medicine*, as well as the psychosomatics program, *How to Communicate in Medicine*. Students can also practice different communication techniques (SPIKES-model) and social skills with the help of SPs in small groups. The programs involving SPs aim to prepare students of medicine during their internship for later contact with real patients during their clinical practice.





Bedside teaching: a history of success

The project, *Bedside Teaching*, was inaugurated in October 2009 in the Clinic for Internal Medicine at the University Medical Center Ulm. This project has as its goal the comprehensive improvement of the practical training of medical students in both their clinical rotation in internal medicine and during their internship year.

The learning objectives are to obtain a complete medical history, perform a complete physical examination, recognize pathological clinical findings, record correct documentation, perform phlebotomies and insert indwelling venous catheters. Other goals include independent evaluation of ECGs, performing a bedside test under supervision, and practicing skills needed for patient education and informed consent. For students in their internship year, the project provides two additional seminars conducted exclusively at the bedside to supplement the previously offered seminars. The following didactic components were implemented in small groups: an introductory course (*Skills Lab*); teaching rounds (*Findings Exchange*); structured practice at ECG evaluation; a bedside test; and patient education/informed consent. Student progress was documented using a log with regular monitoring of entries. One objective that remains to be implemented is to assess student skills using an objective structured clinical examination (OSCE). The specific benefits of the above-described didactic components relate to the systematic approach of teaching basic medical skills at the bedside. Moreover, the continuous supervision of students by a single instructor offers significant advantages. Students in their internship year are offered additional weekly teaching rounds as part of the project. Innovative aspects of these didactic sessions are their high relevance to clinical practice, their interdisciplinary approach within the framework of medical subspecialties and continuous supervision by an instructor.

To date, the reaction from students has been extremely positive: “We think it’s great that there’s someone who has the time to explain things, and can help us with our problems and concerns.” („*Wir finden es gut, dass es jetzt jemanden gibt, der Zeit hat uns die Dinge zu erklären, und an den wir uns wenden können, wenn wir Probleme oder Bedenken haben.*”)

Competence Center of eLearning in Medicine

Within the competence net of medical education in the state of Baden-Württemberg, the Competence Center of eLearning at the Faculty of Medicine plays a significant role. The Competence Center of eLearning has taken on the task of developing long-term strategies for the introduction of new web-based technologies in academic medicine and to realize quality assessment systems, for example, within our complaints and idea management system.

Furthermore, future-oriented studies are today based on a number of different teaching and learning methods. In addition to existing classic elements, we provide the Medical Faculty of Ulm University with eLearning so that the teaching can be more varied, more modern and more flexible. At the same time, students can become more involved by interacting through blogs and forums as well as other appropriate social media tools as part of the teaching process. In addition, the Competence Center of eLearning has developed apps and mobile learning tools for a more modern and contemporary method of teaching.

The Competence Center of eLearning is a central platform for all teachers and students of the Medical Faculty of Ulm University. We assist students in all matters relating to teaching and the use of digital media, and support them in utilizing new media and in creating eLearning and mLearning content.



Theatrum anatomicum

To provide a new teaching facility, the Theatrum anatomicum was established in 2008. In the center of this room there is a mobile operating table which students can view from a nearby observation platform during demonstrations. The state-of-the-art technical equipment includes such features as full HD video transmission, flat screens, a sound system and power-mac while an attached scrub room allows six to eight persons to perform a surgical scrub. Students at Ulm University are instructed in anatomy during the first three consecutive semesters.

First semester medical students are introduced to the subject of general anatomy with demonstrations of the skeletal system, the application of major anatomical principles, and initial hands-on experience with human corpses.

Second semester students, having gained a more complex insight into the human body, are given anatomical presentations emphasizing a deeper understanding of organ systems and their topography.

Third semester students, who have attended the entire anatomy course, benefit further from clinical scenarios. Small group training includes clinical skills, such as suturing, scrubbing, insertion of central venous catheters, tracheal tubes and basic hygiene rules. Clinicians perform example operations and invasive procedures as part of the main anatomy course to underline the relevance of anatomy within the context of basic scientific knowledge. Students assist directly at the operating table under realistic operation conditions.

The Theatrum anatomicum provides the opportunity to allow students to be trained in basic surgical skills and authentic professional behavior, and thus it combines clinical and preclinical education with anatomical surgical procedures and techniques.

Evaluation online

Evaluation is an important aspect of the quality management system of the Medical Faculty of Ulm since it is a means to directly improve the medical curriculum. Since 2011, all medical seminars and lectures, in every clinical and preclinical stage of study, are evaluated online. Supported by a study-related bonus system, an overall response rate of 60% has been achieved throughout all student cohorts.
Additionally, regular evaluation meetings have been held to provide a discussion platform for students, teachers and curriculum developers. Our primary goal is the continuous improvement of the quality of our curriculum in order to safeguard the high standard of training and education for the physicians of tomorrow.

Didactic training for examiners

Oral examinations have always been a crucial assessment format to evaluate and to guarantee the quality of medical education and thereby to secure high quality patient care. To achieve a high level of quality in the oral part of the final examination for our medical students, a training program for oral examiners has been established, in which almost 400 examiners have participated in recent years.

Task Force “Research in Medical Education”

Optimal research in medical education requires optimal support from the Faculty of Medicine. To achieve this, our recently established task force, “Research in Medical Education,” deals with all study and research questions that inevitably arise as a result of innovative curricula, new methods of teaching and learning, and continuous developments in medical education. The main goals of the task force are:

- Quality assurance in teaching
- Qualitative and quantitative improvement in medical education research
- Mentoring and cooperation in educational research projects
- Coordination of different projects in the field of educational research

Homepage:
www.uni-ulm.de/med/fakultaet/forschung/lehrforschung.html

AG LEHR FORSCHUNG
Medizinische Fakultät
Universität Ulm

Dentistry



Global Commitment

The overall aim of the dental education at Ulm University is to produce dentists who are competent at providing patients with independent dental care based on scientific evidence and who are capable of adapting to the rapid changes in technology and new generations of dental products.

Strengthening of Clinical Skills and Competences

A complete revision of the lectures and seminars in preclinical dental subjects has shifted the teaching content from a focus on dental technician lab work towards training in clinically related procedures. This process will be complete following a total overhaul and reorganization of the traditional preclinical courses into an interdisciplinary simulation clinic (skills lab) that started in 2011. The opening ceremony was held on February 5th, 2014.

The teaching practice for the multi-speciality courses in restorative dentistry, endodontics, prosthodontics and periodontology has gone through extensive renovation. It now houses 20 superior dental operatories where dental treatment is delivered by undergraduate dental students. A major characteristic of patient-related dental education is the continuous and ever increasing need to integrate new diagnostic tools and treatment options into the curriculum. In order to relieve students of the burden of meeting the high cost of new instruments, devices and materials, a proportion of the tuition fees has been made available as a fund to supply students with free instruments and materials, such as tray-organized dental instruments for clinical courses, dental working models, model teeth for cavity and crown preparation, and rotary nickel-titanium instruments for root canal preparation.



Recently, patient-based teaching has also been implemented in orthodontics.

A multi-step program, starting with a two-day exploration of the clinical environment during the second year and ending with a clinical traineeship after the third year, has been designed in order to achieve a gentler transition from pre-clinical phantom courses to the treatment of real patients by dental students in the teaching clinic. Activities in the near future will concentrate on the further development of interdisciplinary clinical courses.

Teaching of Modern Treatment Concepts

Clinical teaching covers both proven state-of-the-art methods as well as innovative diagnostic treatment options that include digital radiography, adhesive tooth-colored restorations, full ceramic restorations, non-destructive cavity preparation, root-canal preparation with rotating instruments, and implant-based oral rehabilitation. The focus is on etiology-related treatment strategies and minimal invasion. The teaching of modern clinical concepts is supported by the increasing use of the Medical Faculty's web-based teaching platform MOODLE which offers students the opportunity both to download Powerpoint slides, videos and online self-evaluation tests, and to communicate directly in the "news group."

eLearning – a Tool for Interactive and Case-Based Learning in Orthodontics

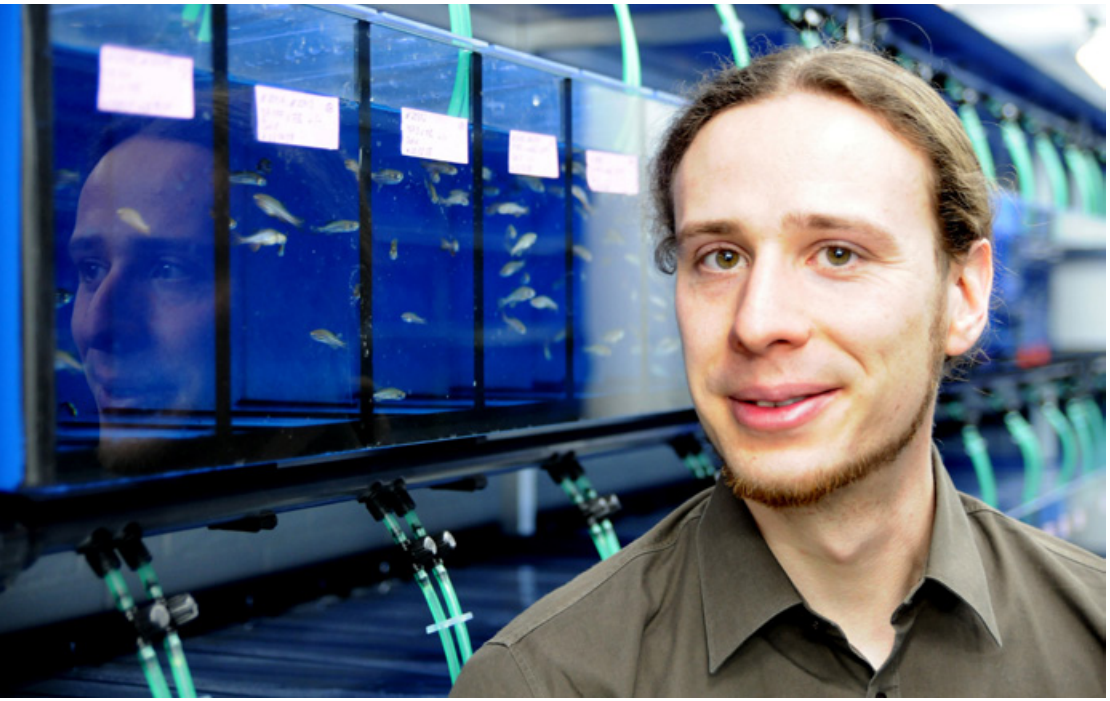
In the Department of Orthodontics, a new eLearning platform for "case-based learning" is currently being developed and tested with the support of tuition fees. The aim of this project is to offer students an interactive PC tool for a virtual case planning on a PC. Evaluation modules for virtual 3D diagnosis (model cast analysis and cephalometric analysis) and case planning are integrated. This program, which is still in the optimization process, offers the opportunity for students to practice independently either complete therapy planning or simply an individual evaluation of results. The program is professionally supported by the company Soon Systems (Ulm). Other cooperation partners contribute their experience concerning digital and three-dimensional analysis and diagnostics.

Caring for Students

Great efforts have been made to improve the mentoring and care of students. The dental school's Teaching Coordinator employed since 2007 has become an essential and indispensable contact for the students as documented by a repeatedly high and positive evaluation. The functions of the Teaching Coordinator are performed in close cooperation with the Dean of Students and the Student's Office, and cover a wide range of services that includes communication with licensing authorities and examination boards, updating and management of timetables, course guidance and counseling, management of the teaching platform MOODLE, registration, teaching evaluation, lecture hall management, surveys among the students, management of teaching assignments, equivalence confirmations, and letters of recommendation.

At the end of each semester, students regularly express their appreciation of the high level of care and mentoring in their evaluation of the teaching being carried out in all courses. Individual supervision and care is promoted as a result of the relatively small group size of 27 students per semester.





Molecular Medicine: Bachelor, Master and PhD Programs

Significance of Molecular Medicine

Scientists working in the field of molecular medicine analyze the molecular mechanisms of disease pathogenesis with the long-term goal of developing innovative diagnostic and therapeutic concepts and strategies. Their experimental findings are highly relevant for society since cardiovascular diseases, infectious diseases, cancer, metabolic disorders, to name but a few, are deemed to be the major causes of death worldwide.

Moreover, dementia, such as Alzheimer's disease and other diseases linked to aging, will seriously increase the costs for our health systems, especially in view of the dramatic demographic changes in population structure. Because of the significance of molecular medicine for modern society, the need to provide highly trained scientists will be of immense relevance for the future.

Bachelor of Science Program

The Bachelor of Science Program lasts six semesters and ends with the completion of a bachelor thesis in the final semester. This course of study combines the topics and questions of experimental medicine with the methods of molecular and cell biology as well as genomics and proteomics. Based on an intensive basic mathematical and natural science education in the first two semesters, the main educational emphases are placed on physiology and pathophysiology of cells and organs. The course of study is oriented towards students who are interested in working in biomedical science, but not necessarily in the direct care of patients. The educational goal is the acquisition of knowledge, capabilities and skills that qualify graduates for employment in the area of research, development and application in biomedicine. The program consists of modules which include anatomy, biochemistry, bioinformatics, developmental biology, gene therapy, human genetics, immunology, microbiology and virology, oncology, pathology, pharmacology and toxicology, and physiology.

The Bachelor's program starts in the winter semester and offers 50 study places. Applicants are chosen on the basis of their results at undergraduate level. Good marks in the natural sciences, mathematics and English will increase the chances of obtaining a study place. About 900 persons apply for this program each year.

Master of Science Program

The Master of Science program is based on a basic bachelor's biomedical course of study and the educational aim of this master's course of studies is to prepare graduates for independent scientific work on a biomedical topic.

The master's course of study in molecular medicine is research-oriented and, due to constantly increasing internationalization, is conducted in English. Core elements of the master's course of studies consist of practical research training courses (lab rotations, elective course area) over a period of several weeks in the first year of studies in which students must concern themselves with current research topics and new scientific methods. The plan of studies also includes courses on good scientific and laboratory practice, bioethics, project management and funding as well patent law.

Due largely to the abolition of the traditional semester structure, students can already acquire their master's degree in this intensive course of study after one and a half years.

Fast Track Promotion opportunity

Highly motivated and talented students have the opportunity to enter directly into the three-year doctoral phase within the International PhD program in Molecular Medicine. The master's course of study in molecular medicine prepares them for the International PhD program conferring the degree of Doctor of Philosophy (PhD) or Doctor rerum naturalium (Dr. rer. nat.). Students with above-average qualifications are given the opportunity after the end of the first year of study to directly enter the three-year doctoral phase (Master/PhD program). Such an opportunity makes this master's program a highly attractive option for outstanding students.

PhD Program

Based on the results of a biomedical master's course of studies, the aim of the PhD course is to train postgraduates by means of a structured program to allow them to carry out scientific research independently and on their own initiative in the field of molecular medicine. Successful completion of the PhD program results in being awarded the degree of Doctor of Philosophy (PhD) or Doctor rerum naturalium (Dr. rer. nat.).

The PhD program is internationally-oriented and conducted in English. The central element is the three-year doctoral dissertation at the end of which the student must defend his/her research results in open disputation before a scientific committee. Each doctoral student is supervised by a three-member supervisory team. Apart from laboratory work, doctoral students must attend compulsory courses. These include, for example, the lecture series, Improve your Textbook Knowledge, practical laboratory training courses and a seminar series such as a Journal Club or Progress Report. A large variety of Key Competence Seminars are also offered on a voluntary basis.

The PhD program is an integral part of the International Graduate School in Molecular Medicine Ulm which is funded by the Excellence Initiative of the German federal and state governments (see also page 56).

Proven quality

The Bachelor, Master and PhD programs have each been successfully accredited by the Central Evaluation and Accreditation Agency of Hannover (Zentrale Evaluations- und Akkreditierungsagentur Hannover). This accreditation attests to the high scientific and educational quality of all three programs.



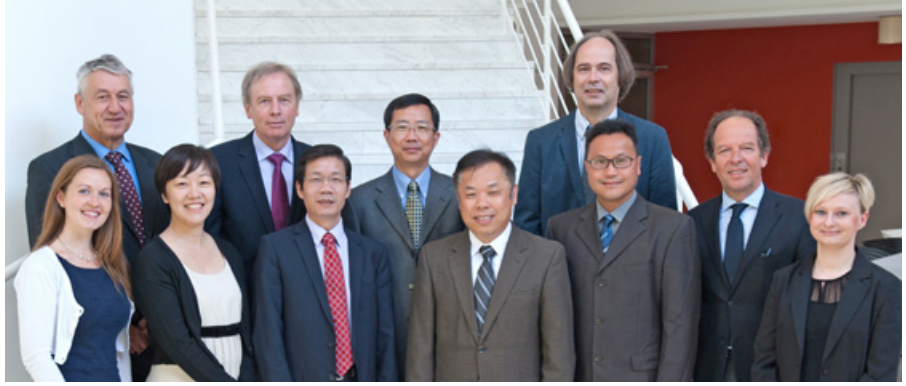
International Cooperations
Gender Equality Policies



International Cooperations of the International Graduate School in Molecular Medicine Ulm.

International Cooperations

Scientific excellence not only depends on the outstanding performance of researchers and teachers but also on the close cooperation with a worldwide network of renowned partner institutions. In addition to the increasing level of personal interaction between researchers of Ulm University Medicine and expert institutions abroad, and their participation in collaborative research projects and networks coordinated by institutes in the USA and European countries, we have established several international research and training networks. These networks, such as the “European Huntington’s Disease Network” (EHDN; see page 46), are funded, for instance, by the EU and CHDI Foundation.



The International Graduate School in Molecular Medicine (see page 56) has made every effort to develop doctoral training programs within an international context. Consequently, the Graduate School has established close links with the following international partner institutions since its foundation in 2006:

- Biocenter Oulu, Finland (mutual exchange programs and summer schools, joint PhD program)
- Padua, Italy (joint PhD program)
- Bart's and Queen Mary's College (London), Universitã Campus Bio-Medico di Roma (Rome), Universitat autõnoma de Barcelona (Barcelona) (tri-national PhD program in Endocrinology)
- University of North Carolina at Chapel Hill, USA (common research projects between PhD students, exchange programs, summer schools)
- Huazhong University of Science and Technology/Tongji Medical College, Wuhan, China (summer schools)
- Beijing, China (summer school)
- Johns Hopkins University School of Medicine in Baltimore, USA (guest professor Philip Wong)
- University of Tokyo, Japan (guest professor Hiromitsu Nakauchi)

With the aid of various exchange programs, Ulm University makes it possible for students of medicine, dentistry and molecular medicine to complete a part of their course of studies in foreign universities cooperating with Ulm, for instance:

- Universidade Federal Fluminense Niteroi, Brazil
- Universidade do Estado do Rio de Janeiro, Brazil
- Universidad Católica de la Santísima Concepción, Chile
- Southeast University Medical College, Nanjing, China
- Tongji University, Shanghai, China
- Tongji Medical College of the Huazhong University, Wuhan, China
- Kwame Nkrumah University of Science and Technology, School of Medicine, Kumasi, Ghana
- Semmelweis University, Budapest, Hungary
- Albert-Szent-Györgi University, Szeged, Hungary
- University of Massachusetts Medical School, Worcester, USA
- University of North Carolina at Greensboro, Greensboro, USA
- Western University, Middletown, USA
- Southern Connecticut State University, New Heaven, USA
- Portland State University, Portland, USA
- University of Connecticut, Storrs, USA
- University of Newcastle, Australia

Within the framework of the Erasmus exchange program, Ulm University has close links with the following partner universities:

- University of Liverpool, UK
- Medizinische Universität Innsbruck, Austria
- University of Oulu, Finland
- Université d'Angers, France
- Université de Franche Comté, Besançon, France
- Université Paris 13 – Paris Nord, France
- Università degli Studi di Padova, Italy
- Università Campus Bio Medico di Roma, Italy
- Università degli studi di Napoli, Italy
- Università degli Studi di Cagliari, Italy
- Univerzita Komenského v Bratislave, Bratislava, Slovakia
- Lithuanian University of Health Sciences, Kaunas, Lithuania
- Universita Karlova v Praze, Praque, Czech Republic
- Universidad de Málaga, Spain
- Universidad de Las Palmas de Gran Canaria, Spain
- Universidad de La Laguna, Santa Cruz de Tenerife, Spain
- Universidad de Sevilla, Spain
- Universidade Nova de Lisboa, Lisbon, Portugal
- Universiteit Leiden, Netherlands
- T.C. Maltepe Üniversitesi, Istanbul, Turkey



Zertifikat seit 2008
audit familiengerechte hochschule

Gender Equality Policies

In April 2008, the Ulm University Medical Center was the first University Hospital in Baden-Württemberg to receive the Career and Family certificate from the Hertie Foundation;

Ulm University followed in November 2008 by being awarded the Family-friendly University certificate and since then numerous provisions, for example, flexible working hours, opportunities for leadership development, practical information for employees returning to work following a family-related career break, have been gradually introduced and implemented.

Gender equality is an important goal of Ulm University and has been fixed in its “Plan for Structure and Development.” Ulm University strictly supports the DFG concept of “Research-oriented standards of gender equality” (see www.dfg.de/chancen-gleichheit). A variety of gender equality measures are anchored in all the boards and panels of the university in the form of the Gender Equality Officer and the newly founded Gender Board. In addition, Ulm University established a new administrative office for Human Resources, Gender and Diversity. One major aim of these measures is to significantly increase the number of females at all levels of leading positions. Ulm University has been ranked in second place (out of 65 universities) with respect to gender aspects in a report of the CEWS (A. Löther, GESIS - Leibniz-Institut für Sozialwissenschaften, Center of Excellence Woman and Science, Hochschulranking nach Gleichstellungsaspekten, 2009, Bonn).

Ulm University and its Medical Center are actively engaged in adopting numerous measures to promote gender equality policies.

Mentoring Program

A special Mentoring and Training program (MuT), which has been in place for several years, supports female students, doctoral candidates, and post-doctoral researchers in planning their careers, in order to prepare them for their future leadership roles in science and thus to improve their career prospects. Many of the mentors who represent the MuT program (Mentoring and Training) have themselves built up a significant career in science while raising their children at the same time, and therefore act as role models for young women in similar situations.

Margarete von Wrangell Post-Doctoral Program for Women in the State of Baden-Württemberg

This program fosters the postdoctoral theses of female scientists. The grant support lasts for up to five years, three of which are funded by the Ministry of Science, Research and the Arts, and two by Ulm University.

Schlieben-Lange Program for Young Women Scientists with Children

Within the framework of this special program, Ulm University awards scholarships for young women scientists with children on behalf of the State Government of Baden-Württemberg and the European Social Fund. The aim of this program is to increase the number of women with children who can attain professorships by improving the compatibility of the scientific qualification phase with their family responsibilities.





Katja Schilling, Vera Gramich, Dr. Melanie Schirmer, and Dr. Nicole V. S. Ratzinger (from left to right) received the Mileva Einstein-Marić-Award of Ulm University in February 2012.



Mileva Einstein-Marić Award

Since 1999, Ulm University has granted a Women's Award (now known as the Mileva Einstein-Marić Award) worth €5,000. On the one hand, this prize can be used to acknowledge and support special structural measures and innovative projects for the effective promotion of women and, on the other hand, to recognize excellent scientific performance by nominating individuals for this prize. The presidential council of the university decides on the winner of the prize based on the recommendations of the Equal Opportunities Commission.

The Medical Faculty's Intramural Support Program

Finally, there is specific support for female scientists within the Medical Faculty's Modular Program. Within both the Individual Grants and the Rotation Position programs, special conditions apply for mothers in order to improve their chances of acquiring these research funds.

Child Care Center – In the summer of 2007, the completion of a new child day care center brought an important structural improvement to the Medical Center and the university where up to 70 children between the ages of nine weeks and three years can now be cared for (chère/crib). Moreover, the construction of a new kindergarten was begun in 2010 and opened in September 2011 for the care of 100 children aged from three years to school age. As a rule, the centers are not closed for more than five days in the year in order to support our qualified employees to reconcile the needs of their families and careers more effectively. In the Flea Circus, the Student Welfare Service's child day care center, there are 20 places for one to three-year old children of enrolled graduate and postgraduate students. Many kindergartens in the surrounding area also look after children between the ages of three and six years.

In order to enable PhD students with children to pursue their work, the International Graduate School in Molecular Medicine Ulm offers various childcare programs. It provides financial support for childcare during meetings and conferences, stays abroad and for childcare services outside the regular business hours of day care centres. Practical help in finding the right day care center can also be offered. For doctoral candidates who are pregnant, the Graduate School finances the employment of technical assistants (up to one year) to conduct experiments for students during pregnancy and maternity leave as regulated by law.

Hertha Nathorff Program

This recently established program enables the scientific career development of young female scientists with a PhD or MD background. Through a total exemption from clinical obligations, junior female scientists are encouraged to conduct experimental (preferred) or clinical studies. In addition, technical assistance can also be funded to secure part-time work arrangements for the participant. Further individual requirements for additional qualifications (e.g. conference visits, networking etc.) are also eligible for financing. The criteria for receiving a grant are a successfully completed doctorate and an innovative research topic, which is preferably integrated into the research focus of the Medical Faculty and the CRC Initiative. In 2014, funding has been allocated for up to seven positions.

Holiday Care Programs

Holiday care programs for children of employees of the Medical Center and the University have been taking place since 2006. Supervised throughout the day and grouped according to age and school year, the children are able to make their first contact with a variety of scientific fields over a period of three weeks during the Easter and summer vacation. For primary school children and those about to start school, there are what are known as Research Holidays while for children in their fifth, sixth and seventh year of school, there is the Science Camp. In the Science Camps children attend lectures and practice research in workshops under the guidance of scientists, students performing their lectureships and voluntary senior consultants. These programs have proved to be hugely popular and are a welcome source of support for parents of school-age children during the holiday period.





Departments and Institutes

Ulm University Medicine is comprised of 10 preclinical institutes, 11 clinical-theoretical institutes, 34 medical institutes and departments and 3 co-opted institutes. Some of these have been combined to create Medical Centers. The institutes and departments are described on the following pages.

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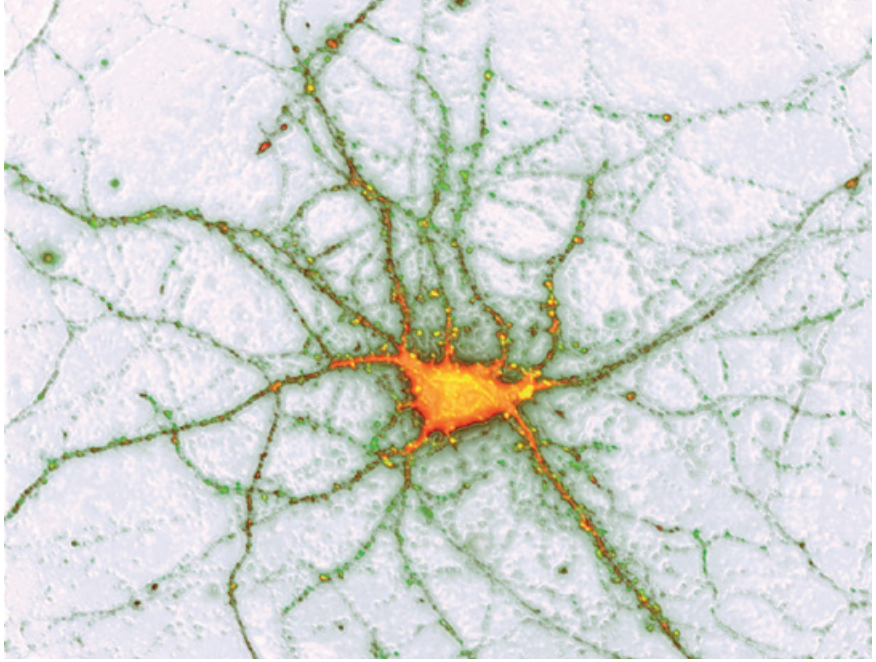

Hippocampal neuron in culture immunostained for a dendritic marker (red) and a synaptic molecule (Abi-1) in green.

Institute of Anatomy and Cell Biology

Head of Institute: Prof. Dr. Tobias M. Böckers

Keywords: Cell adhesion | heat shock proteins | neurogenesis | stem cells | synapses

The Institute of Anatomy and Cell Biology is concerned with research in the area of molecular neuroscience and teaches human anatomy to students studying molecular medicine, medicine and dentistry. The *prosektur* is also part of the institute. It has in all about 30 employees among whom are two professors (Prof. Tobias M. Böckers and Prof. Nikola Golenhofen), postdocs, PhD students and several medical students.

Our research topics concentrate on synaptic contacts within the central nervous system. Glutamatergic synapses in the central nervous system are specific cellular junctions that are characterized by synaptic vesicles attached to the active zone of the presynapse and an electron-dense web underneath the postsynaptic membrane known as the postsynaptic density (PSD). The pre- and postsynaptic membranes are interconnected by synaptic cell adhesion proteins (i.e. neurexin-neuroligin, cadherins) that are analyzed in the lab. PSDs are composed of a dense network of several hundred different proteins that creates a macromolecular complex serving a wide range of different functions. Prominent PSD proteins, such as members of the MaGuk or ProSAP/Shank family, build up a dense scaffold that creates an interface between clustered membrane-bound receptors, cell adhesion molecules and the actin-based cytoskeleton. The synaptic rearrangement (structural

plasticity) is a rapid process and is believed to underlie learning and memory formation. The characterization of synapse/PSD proteins is especially important in light of recent data that suggest that several mental disorders have their molecular defect at the synapse/PSD level. The generation of induced pluripotent cells (iPS cells) from patients that can be differentiated into neurons of different kinds will help in understanding the pathophysiology of neuropsychiatric disorders.

The research group of Prof. Golenhofen investigates the role of several cell adhesion molecules within synaptic contact zones during development and plastic changes. Moreover, the group elucidates the physiological function of heat shock proteins in neurons, with respect to degeneration and regeneration, as well as in different neurological disease models.



Teaching anatomy in the newly built *Theatrum anatomicum* neighboring the dissection room.

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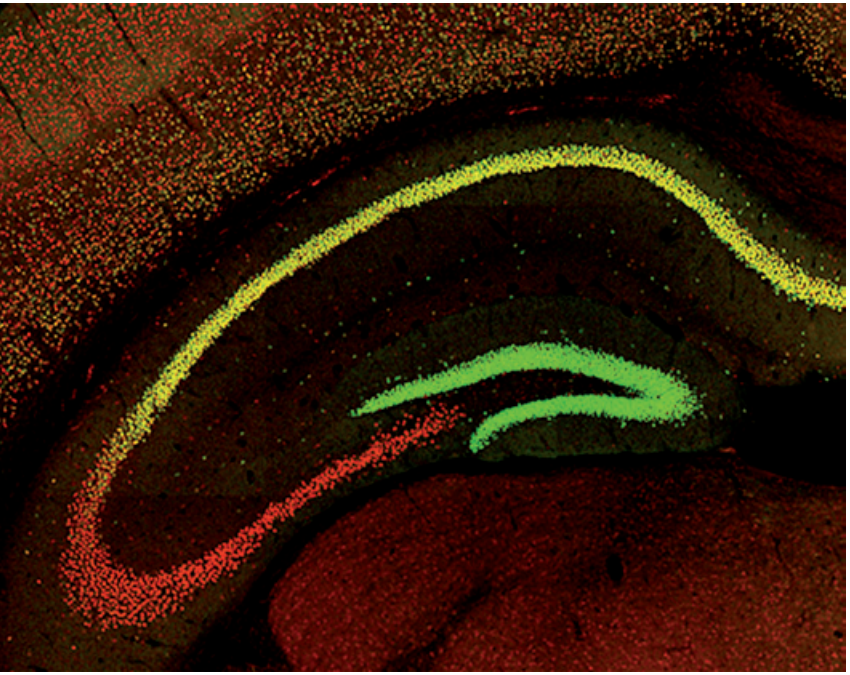
Selected Publications:

- *Jannetti L, Grabrucker St, Eckert M, Chhabra R, Pfänder St, Mangus K, Ehret G, Boeckers TM, Grabrucker AM Zinc deficiency dysregulates the synaptic ProSAP/Shank scaffold and might contribute to the severity of autism spectrum disorders. Brain 137 (Pt 1):137-52 (2014) .*
- *Kleijer K; Schmeisser M; Krueger D; Boeckers T; Scheiffele P; Bourgeron T; Brose N; Burbach J. P Neurobiology of autism gene products: towards pathogenesis and drug targets. Psychopharmacology 231(6):1037-62 (2014)*
- *Schmeisser MJ, Baumann B, Johannsen S, Vindedal GM, Jensen V, Hvalby Ø, Sprengel R, Seither J, Lattke M, Oswald F, Boeckers TM and Wirth T IKK/NF-κB signaling dynamically regulates synapse formation and spine maturation via Igf2/Igf2R. J Neurosci 32(16):5688-5703 (2012).*
- *Schmeisser MJ, Ey E, Wegener St, Kuebler A, Bockmann J, Shiban E, Spilker C, Balschun D, Skryabin BV, tom Dieck S, Smalla KH, Montag D, Leblond C, Faure P, Torquet N, Le Sourd AM, Stempel V, Shoichet S, Schmitz D, Kreutz MR, Bourgeron T, Gundelfinger ED and Boeckers TM Autistic-like behaviours and hyperactivity in mice lacking ProSAP1/Shank2. Nature, 486: 256-260 (2012).*
- *Schmeisser MJ and Boeckers TM Shank1 and Prosap1/Shank2 Mouse Models of Autism. Autism Volume 2, 4; 1000106 (2013).*



Cross section through the adult mouse hippocampus. Expression of the transcription factors Bcl11a/CTIP1 (red) and Bcl11b/CTIP2 (green) is visualized by employing specific antibodies against these proteins.

Institute of Molecular and Cellular Anatomy

Head of Institute: Prof. Dr. Stefan Britsch

Keywords: transcription factors | hippocampus | spinal cord | microRNA | spines | dendrites

Research Group: Transcriptional Control of Neural Development

Head: Prof. Dr. Stefan Britsch

The ability of the mature nervous system to integrate, compute and distribute information is based on developmental processes that create diversity, connectivity and the spatial organization of neurons. We are interested in the identification and functional characterization of transcriptional networks regulating these processes. Recent work from our group demonstrated that the zinc finger transcription factors Bcl11a/CTIP1 and Bcl11b/CTIP2 are critical regulators of neural development.

Hippocampal Neurogenesis

The development of the hippocampus, a major brain structure involved in learning and memory, starts early in embryogenesis and continues postnatally. The dentate gyrus, the primary gateway for input information into the hippocampus, is one of only two brain regions with continuous neurogenesis in adult mammals. We found that Bcl11b, as expressed in postmitotic cells, is required for postnatal development as well as adult neurogenesis of the dentate gyrus. Our data reveal phase-specific functions of Bcl11b demonstrated by feedback control of the progenitor cell compartment as well as a cell-autonomous arrest of neuronal differentiation leading to impaired learning and memory behavior. Further studies will focus on elucidating the mechanism of Bcl11b regulation of neurogenesis and its role in neurodegenerative diseases as well as in the aging process.

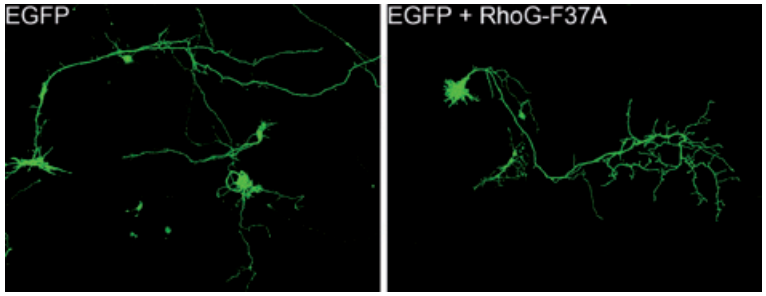


Fig. 2 Transfected hippocampal neurons in cell culture were visualized by staining for the enhanced green fluorescent protein (EGFP). Neurons expressing the dominant-negative RhoG construct RhoG-F37A (right panel) display much more axonal branching than control neurons (left panel).

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Dorsal Spinal Cord Development

Dorsal spinal cord neurons receive and integrate somatosensory information provided by neurons located in dorsal root ganglia. We uncovered that Bcl11a is essential for development of the dorsal spinal cord. Conditional ablation of the Bcl11a gene in mice revealed that dorsal spinal neurons require Bcl11a for terminal differentiation and morphogenesis. Moreover, a subset of cutaneous sensory afferents depends on Bcl11a in postsynaptic spinal target neurons to be able to grow into the dorsal horn and to form neuron circuits. Using transcriptome analysis and ChIP-on-embryos we identified the secreted frizzled-related protein-3 (sFRP3, Frzb) as a direct transcriptional target of Bcl11a in spinal neurons. Phenotypes of both, Bcl11a and Frzb deficient dorsal spinal cords, overlap demonstrating Frzb to be a functional downstream component of Bcl11a-dependent regulatory pathways in spinal neurons.

Research Group: Molecular Mechanisms of Neuronal Connectivity

Head: Prof. Dr. Stefan Schumacher

MicroRNAs are small noncoding RNAs which posttranslationally regulate gene expression. They are likely to have key roles in neuronal development and plasticity. We are interested in microRNA targets that contribute to the establishment of proper neuronal connectivity. Our focus is on the function of the small GTPase RhoG, the expression of which is regulated by the microRNA miR-124. This microRNA is specifically expressed in the nervous system. We found that miR-124-regulated RhoG inhibits axonal branching acting via an ELMO/Dock180/Rac1 signaling pathway. Additionally, RhoG was shown to reduce dendritic branching in a Cdc42-dependent manner. Thus, RhoG emerges as a cellular conductor of Rac1 and Cdc42 activity, in turn regulated by miR-124 to control axonal and dendritic branching.

Selected Publications:

- *Del Barrio MG, Bourane S, Grossmann K, Schüle R, Britsch S, O' Leary DDM, Goulding M (2013) A transcription factor code defines nine sensory interneuron subtypes in the mechanosensory area of the spinal cord. PLoS ONE 8(11): e77928.*
- *Simon R, Brylka H, Schwegler H, Venkataramanappa S, Andratschke J, Wiegreffe C, Liu P, Fuchs E, Jenkins NA, Copeland NG, Birchmeier C, Britsch S (2012) A dual function of Bcl11b/Ctip2 in hippocampal neurogenesis. EMBO J 31: 2922-2936.*
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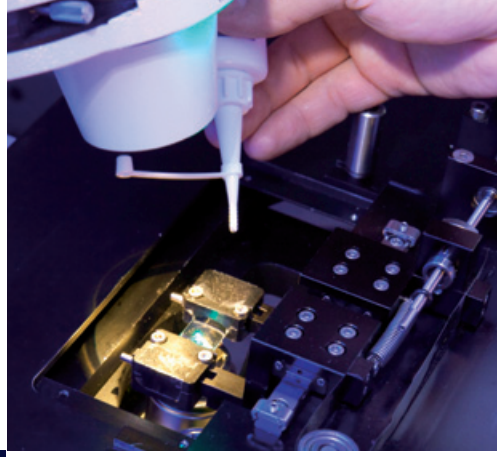


Computer-controlled cell stretch device mounted on the stage of an inverted microscope. Lung cells are grown on the silastic membrane on top of the objective.



Institute of General Physiology

Head of Institute: Prof. Dr. Paul Dietl

Keywords: epithelial transport | exocytosis | ion channels | lung | purinergic signaling

Research Group: Pulmonary Alveolar Physiology and Pathophysiology

Head: Prof. Dr. Paul Dietl

The pulmonary alveolus is a unique structure that dwells in a delicate micro-environment between air and blood. With a diameter of about 200 mm, each alveolus contains a highly curved air-liquid interface, which has the tendency to collapse and makes the lung an intrinsically unstable organ. To prevent alveolar collapse, epithelial cells must secrete surfactant, a lipid-rich, lipoprotein-like substance, stored within so-called “lamellar bodies,” the storage vesicles of pulmonary epithelial type II pneumocytes. In addition, alveolar epithelial cells must continuously reabsorb electrolytes and water to keep the alveolus “dry.”

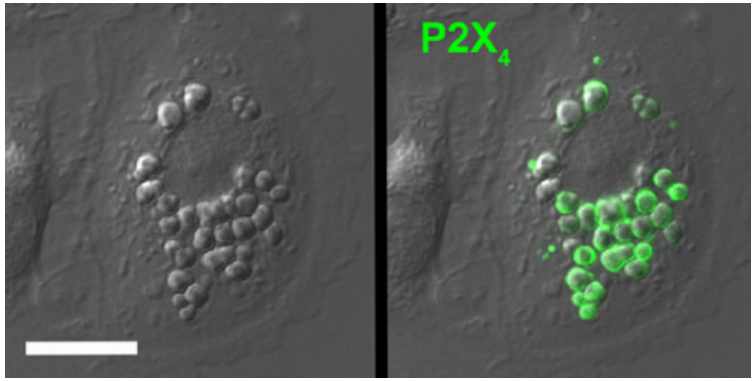
Aiming at an integrative approach using primary epithelial cell cultures on permeable and flexible membranes, the group investigates mechanisms of cellular mechanotransduction (stress – response coupling), Ca2+ signaling, electrolyte transport (Ussing chamber), fluid reabsorption (D2O dilution method) and surfactant transformation at the air-liquid interface (inverted interface).

Research Group: Molecular Mechanisms of Cellular Secretion

Head: Prof. Dr. Manfred Frick

Our lab is interested in the molecular mechanisms that regulate cellular secretion. Regulated secretion is a fundamental process in almost all types of eukaryotic cells. In particular, we study secretion of pulmonary surfactant. Pulmonary surfactant is secreted via exocytosis of lamellar bodies and constitutes an ideal model to study cellular secretion of large macromolecular complexes. We use high-resolution, live-cell imaging techniques to investigate molecular mechanisms that regulate individual stages of the exocytic secretion process – from initiation of membrane fusion to post-fusion vesicle compression. Overall, it is our aim to provide a mechanistic model of the sequential molecular interactions that are necessary for efficient secretion of macromolecular complexes.

In addition, we are interested in the role of purinergic signaling for maintaining alveolar homeostasis. Encouraged by a recent discovery that lamellar body exocytosis, surfactant secretion and fluid resorption in the alveolus are intimately linked via purinergic signaling we want to further elucidate the role of purinergic receptor activation for maintaining alveolar homeostasis under physiological and pathological conditions.



Purinergic receptors (green) are expressed on lamellar bodies in a primary alveolar type II pneumocyte.
From Miklavc et al, PNAS 2011.

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Selected Publications:

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- *Fois G, Weimer M, Busch T, Felder ET, Oswald F, von Wichert G, Seufferlein T, Dietl P, Felder E (2013): Effects of keratin phosphorylation on the mechanical properties of keratin filaments in living cells. FASEB J 27:1322-9.*
- *Miklavc P, Hecht E, Hobi N, Wittekindt OH, Dietl P, Kranz C, Frick M (2012): Actin coating and compression of fused secretory vesicles are essential for surfactant secretion--a role for Rho, formins and myosin II. J Cell Sci 125:2765-74.*
- *Miklavc P, Mair N, Wittekindt OH, Haller T, Dietl P, Felder E, Timmler M, Frick M (2011): Fusion-activated Ca2+ entry via vesicular P2X4 receptors promotes fusion pore opening and exocytotic content release in pneumocytes. Proc Natl Acad Sci U S A 108:14503-8.*



UV laser microdissection of individual neurons.

Institute of Applied Physiology

Head of Institute: Prof. Dr. Birgit Liss

Keywords: dopamine | ion-channels & receptors | electrophysiology | molecular medicine | aging and disease

Research Group: Molecular Neurophysiology

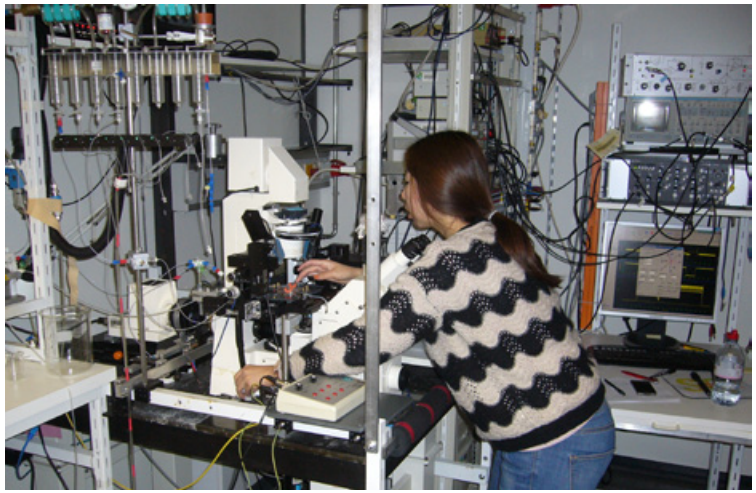
Prof. Dr. Birgit Liss

Our research is focused on the dopamine midbrain system. This system is not only involved in motor control and neurodegenerative disorders, like Parkinson's disease (PD), but it is also crucial for emotional and cognitive brain functions and related disorders, like schizophrenia, drug addiction, or attention-deficit hyperactivity-disorder (ADHD). Our central aim is to define molecular mechanisms and signaling pathways that control cell-specific dopaminergic activity and selective pathophysiology of the dopamine midbrain system, in particular, in aging and PD. To address these issues, we analyze function and molecular biology of individual neurons at different ages from mouse-models, as well as from *post mortem* human brains. We do this by combining functional analysis (electroyphysiology, calcium-imaging) with molecular techniques (UV-lasermicrodissection, quantitative RNA, DNA, and protein analysis) at the level of individual cells. We focus on ion-channels and receptors since their cell-specific activity directly defines individual neuronal activity patterns in health and disease. We aim to define new potential targets for the development of novel, more specific pharmacological therapeutic strategies for distinct diseases of the dopamine system.

Research Groups: Potassium Channels and Calcium Signaling

Prof. Dr. Stephan Grissmer & PD Dr. Werner Melzer

Our overall aim is to guide rational drug design to be specific for each ion channel type and for the therapy of related diseases.
We analyze properties, modifications and modulations of ion channels and receptors in the context of their roles in cellular function in health and diseases. We use molecular biological techniques in combination with electrophysiology to study structure function relationships of potassium channels with the goal of designing drugs for the modulation of ion channel function. We used different modifiers of potassium channels in combination with site-directed mutagenesis to identify the availability of the binding sites in different states of the channels. We also investigate mechanisms of excitation-contraction (EC) coupling in skeletal muscle. We focus on the release of calcium ions stored in the sarcoplasmic reticulum (SR) that initiates the motor activity of muscle. Changes in the EC coupling are observed in aging, in muscle fatigue and in certain diseases. Point mutations in the ryanodine receptor (RyR), the ion channel that releases calcium from the SR under the control of cell membrane voltage, can lead to malignant hyperthermia (MH) or central core disease (CCD). We are studying the functional alterations of EC coupling using single muscle fibers of mice expressing human RyR mutations.



Yuan Pan (graduate student of the Melzer group) at her experimental setup. She measures calcium signals and electrical currents from isolated muscle cells while controlling the membrane voltage of the cell.

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Selected Publications:

- *Dragicevic E, Poetschke C, Duda J, Schlaudraff F, Lammel S, Schiemann J, Fauler M, Hetzel A, Watanabe M, Lujan R, Malenka RC, Striessnig J, Liss B (2014). Cav1.3 channels control D2-autoreceptor responses via NCS-1 in substantia nigra dopamine neurons. Brain. Jun 16.*
- *Schlaudraff F, Gründemann J, Fauler M, Dragicevic E, Hardy J, Liss B (2014). Orchestrated increase of dopamine and PARK mRNAs but not miR-133b in dopamine neurons in Parkinson's disease. Neurobiol Aging. 35(10):2302-15.*
- *Schiemann J, Schlaudraff F, Klose V, Bingmer M, Seino S, Magill PJ, Zaghloul KA, Schneider G, Liss B*, Roeper J* (2012). K-ATP channels in dopamine substantia nigra neurons control bursting and novelty-induced exploration. Nature Neuroscience. 15(9):1272-80.*
- *Nikouee A, Janbein M, Grissmer S (2012). Verapamil- and state-dependent effect of 2-aminoethylmethanethiosulphonate (MTSEA) on hK(v)1.3 channels. Br J Pharmacol. 167(6):1378-88.*
- *Prütting S, Grissmer S. 2011. A novel current pathway parallel to the central pore in a mutant voltage-gated potassium channel. Journal of Biological Chemistry 286:20031-20042.*



Fig.1: Speakers of ZSE (Center of Excellence for Rare Diseases) opening ceremony:
(from left to right) PD Dr. Holger Cario (Vice Chairman of ZSE); Prof. Dr. Hermann Heimpel (†2014); Prof. Dr. Frank Lehmann-Horn (Chairman of ZSE); Eva Luise Köhler (Patron ACHSE e.V.); Dr. Steve Groft (National Institute of Health, Washington, DC); Prof. Dr. Klaus-Michael Debatin (Head of the Department of Pediatrics and Adolescent Medicine), and PD Dr. Karin Jurkat-Rott (Scientific Secretary of ZSE).

Division of Neurophysiology

Head of Division: Prof. Dr. Dr.h.c. Frank Lehmann-Horn, Senior Research Professor for Neurosciences of the non-profit Hertie-Foundation

Keywords: Translational research on channelopathies | periodic paralyses | Duchenne muscular dystrophy | ^{23}Na magnetic resonance imaging | Rare Disease Center

Our institute employs 14 members, of whom 50% are women. Native languages differ from German by 21%. Four PhD students and seven members contribute to the organization of the *Zentrum Seltene Erkrankungen* (ZSE) (“Center for Rare Diseases”) in Ulm which opened in September 2011 and celebrated its first anniversary in June 2012 (Fig.1).

Translational Research on Channelopathies

Through genetic linkage studies, candidate gene approach and exome sequencing, we identify genes for diseases in which we have detected altered channel function by electrophysiological methods. We clarify their pathogenesis on the molecular level by functional expression of the mutant channels using the patch clamp technique. Then we try to identify pharmaceutics on the market which counteract the mutation effects. Finally, we administer appropriate compounds to patients by off-label use.

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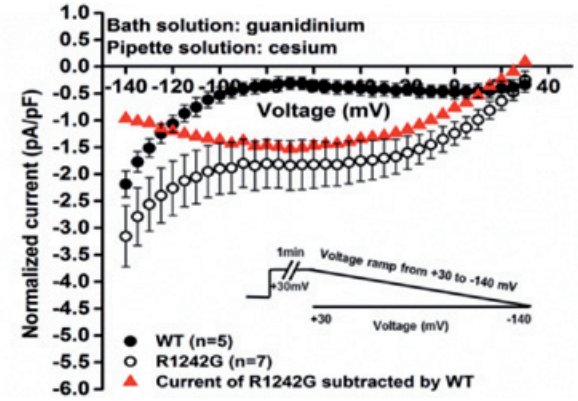
A scientific highlight was the first description of a genetic form of a compartment syndrome characterized by muscle swelling, electrically silent contractures and drop foot after moderate exercise. Sequencing of genes involved in the initiation of muscle contraction identified a missense mutation in the voltage-gated calcium channel, Cav1.1. The mutation is situated in the voltage sensor of the channel. One of the remarkable findings is a short circuit through this channel as a consequence of the mutation (Fan et al. 2013) (Fig.1).

An academic highlight was the Gaetano Conte Award for Basic Muscle Research given to PD Karin Jurkat-Rott in Athens in October 2013.

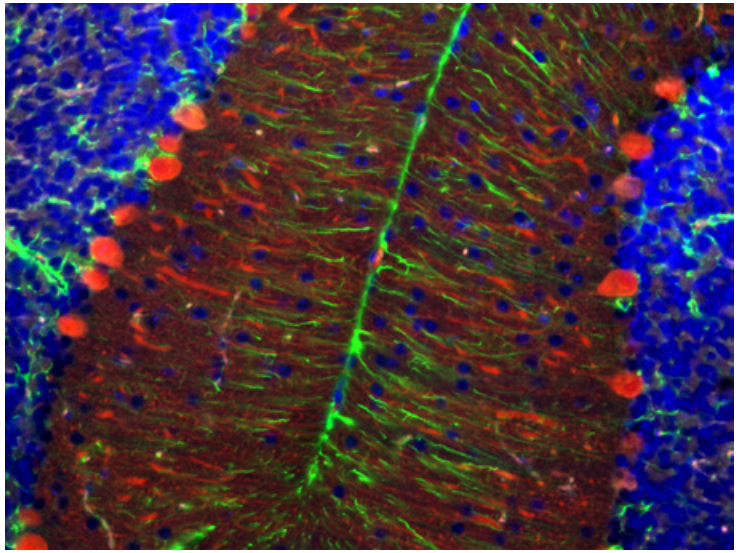
Several advocacy groups have listed our address as channelopathy experts. This motivated us to initiate the ZSE which we organize on behalf of the University Hospital Ulm.



Responses of WT and mutant R1242G channels to an electric ramp (1 min pre-depolarization to +30 mV followed by a ramp from +30 mV to -140 mV over 7 s). The red triangles represent the short circuit. Subtraction of linear passive current was done by holding potential at -90 mV. Data are shown as means ± SEM. Notable is the voltage across the membrane.

Selected Publications:

- *Fan C, Lehmann-Horn F, Weber MA, Bednarz M, Groome JR, Jonsson MKB, Jurkat-Rott K (2013): Transient compartment-like syndrome and normokalaemic periodic paralysis due to a Cav1.1 mutation. Brain, 136: 3775-3786.*
  This publication was selected as paper of the month by the BMBF.
- *Yang R, Jurkat-Rott K, Cao J, Wang G, Seelig HP, Yang C, Liu G, Pan L, Zheng H, Lehmann-Horn F (2013): Hypokalemic periodic paralysis induced by thymic hyperplasia and relieved by thymectomy. JAMA Neurology, 70: 1436-1439.*
- *Amarteifio E, Nagel AM, Weber MA, Jurkat-Rott K, Lehmann-Horn F (2012): Hyperkalemic periodic paralysis and permanent weakness: 3-T MR Imaging depicts intracellular 23Na overload. Radiology, 264: 154-163.*
- *Weber MA, Nagel AM, Jurkat-Rott K, Lehmann-Horn F (2011): Sodium (23Na) MRI detects elevated muscular sodium concentration in Duchenne muscular dystrophy. Neurology, 77: 2017-2024.*
- *Lehmann-Horn F, Klingler W, Jurkat-Rott K (2011): Nonanesthetic malignant hyperthermia. Anesthesiology, 115:915-917.*



Neuroinflammation induces neurodegeneration in the mouse cerebellum.

Institute of Physiological Chemistry

Head of Institute: Prof. Dr. Thomas Wirth

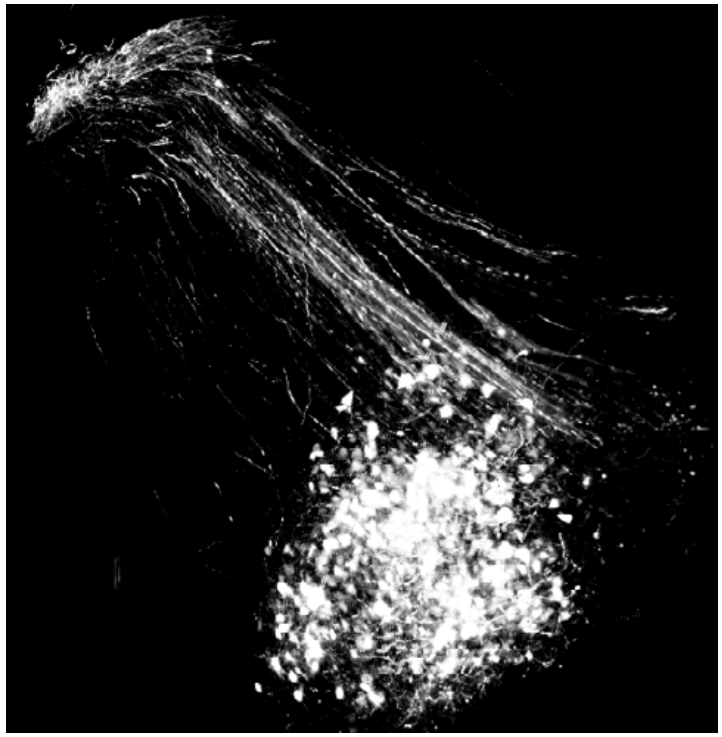
Keywords: NF-κB | Inflammation | SRF | Neurogenesis | Oncogenesis

The Institute of Physiological Chemistry, located in the new life science building of the university, has about 40 members and most of these receive funding from third parties. The research groups of Prof. Wirth and Prof. Knöll study the role of different signaling pathways and transcription factors in development and disease, and both are involved in the teaching of students of medicine, dental medicine, molecular medicine, biochemistry and biology.

Research Group: Signaling in Development and Disease

Head: Prof. Dr. Thomas Wirth

Investigation of the role of IKK/NF-κB signaling in inflammatory processes and the contribution of this pathway to disease development and progression represents a major research program. For these studies we have developed sophisticated genetic tools to allow the analysis of the role of this pathway in mouse models in a conditional way. This means that we can reversibly induce or block this pathway in a cell type/organ-specific manner. We were able to demonstrate that IKK/NF-κB signaling is a driver of inflammatory cardiomyopathy, a disease that is one of the most important causes for heart transplantation in young patients. Furthermore, excess IKK/NF-κB activity in pancreatic b-cells causes inflammatory diabetes mellitus whereas astroglial NF-κB-induction results in neuroinflammation that has variable consequences depending on the onset of inflammation. Likewise, liver fibrosis, a critical predisposition of liver cancer is a consequence of the deregulated activity of this pathway. Furthermore, we could show that IKK/NF-κB signaling is essential in a mouse model of pancreatic adenocarcinoma. We are also interested in the gene regulatory networks governing development and differentiation of lymphoid subpopulations and their dysregulation in immune deficiency syndromes. Finally, a research team at the institute studies the molecular pathways associated with lymphoma development with a strong focus on classical Hodgkin's lymphoma.



Motoneurons in the brain (bottom) send out long axons innervating muscles in the face responsible for such functions as facial expression and eye lid movement.

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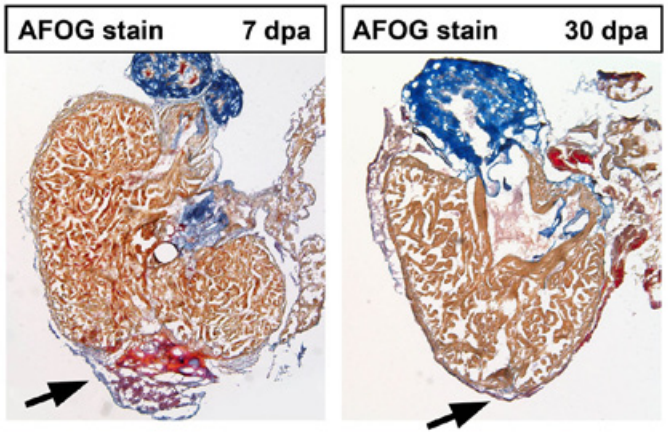
Research Group: Neuronal Gene Expression

Head: Prof. Dr. Bernd Knöll

The research group of Prof. Dr. Bernd Knöll focuses on neuronal gene expression programs during normal as well as pathological nervous system function. We study gene regulatory processes exerted by transcription factors such as SRF (serum response factor) or ATF3 (activating transcription factor 3). During brain development, growing axons navigate towards their final targets in the brain to form functional neuronal networks. In this axon guidance process, we study how SRF interacts with the neuronal cytoskeleton (e.g. microfilaments) to induce changes of neuronal morphology allowing for directed axonal migration. In addition, we study whether gene regulatory processes are targeted by neurodegenerative disorders. For this, we use mouse models for neurological diseases such as epilepsy and multiple sclerosis. Finally, we attempt to apply SRF or ATF3-driven gene transcription to enhance the regeneration potential of transected nerve fibers during axonal regeneration.

Selected Publications:

- *Stern S, Haverkamp S, Sinske D, Tedeschi A, Naumann U, Di Giovanni S, Kochanek S, Nordheim A, Knöll B. (2013). The Transcription Factor Serum Response Factor Stimulates Axon Regeneration through Cytoplasmic Localization and Cofilin Interaction. J Neurosci 33:18836-18848*
- *Sunami, Y., Leithäuser, F., Gul, S., Fiedler, K., Güldiken, N., Espenlaub, S., Holzmann, K.H., Hipp, N., Sindrilaru, A., Luedde, T., Baumann, B., Wissel, S., Kreppel, F., Schneider, M., Scharffetter-Kochanek, K., Kochanek, S., Strnad, P. & Wirth, T. (2012). Hepatic activation of IKK/NF-kB signaling induces liver fibrosis via macrophage-mediated chronic inflammation. Hepatology 56:1117-1128.*
- *Xie, L., Ushmorov, A., Leithäuser, F., Guan, H., Steidl, C., Färbinger, J., Pelzer, C., Vogel, M.J., Maier, H.J., Gascoyne, R.D., Möller, P. & Wirth, T. (2012). FOXO1 is a tumor suppressor in classical Hodgkin lymphoma. Blood 119:3503-3511.*
- *Beck H, Flynn K, Lindenberg KS, Schwarz H, Bradke F, Di Giovanni S, Knöll B. (2012). Serum Response Factor (SRF)-cofilin-actin signaling axis modulates mitochondrial dynamics. Proc.Natl.Acad.Sci U S A 109:E2523-2532.*
- *Maier, H.J., Schips, T.G., Wietelmann, A., Krüger, M., Brunner, C., Sauter, M., Klingel, K., Böttger, T., Braun, T. & Wirth, T. (2012). Cardiomyocyte-specific IKK/NF-kB activation induces reversible inflammatory cardiomyopathy and heart failure. Proc.Natl.Acad.Sci USA 109:11794-11799.*



Zebrafish can fully regenerate their hearts after injury. Histological staining of heart sections at seven days post amputation of the apex of the ventricle shows fibrin-rich wound tissue in red, and resolution of the wound and absence of a collagen-rich scar, which stains blue, at 30 days post amputation.

Institute of Biochemistry and Molecular Biology

Head of Institute: Prof. Dr. Michael Kühl

Keywords: Developmental biology | Regeneration | stem cell biology

Within the Institute we currently have 30 employees, 12 of whom are PhD students. 76.6 % of employees are female and 23.3 % have come from abroad.

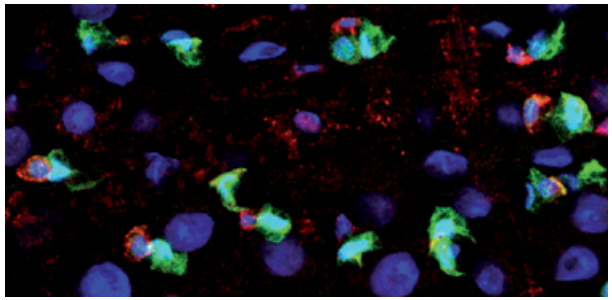
We at the Institute of Biochemistry and Molecular Biology investigate the molecular basis of tissue and organ development during embryogenesis. We also want to learn more about how different tissues and organs are maintained during aging and how they regenerate after injury. To tackle these questions, we use different model organisms such as the mouse *Mus musculus*, the frog *Xenopus laevis*, the fish *Danio rerio*, the fly *Drosophila melanogaster* as well as murine embryonic stem cells.

Several groups within the institute study heart development (Kühl, Pandur and Philipp labs).
The heart is the first functional organ during vertebrate development. Defects during cardiac development result in congenital heart diseases occurring in approximately 1% of all newborns and are estimated to be the cause of 10% of stillbirths and spontaneous abortions. Defects in regulatory molecules that function in early heart development have been linked to congenital cardiovascular malformation. Detailed analyses of normal heart development at the molecular level will help us to understand the pathological changes that occur in congenital heart diseases. Moreover, the recent identification of adult cardiac stem cells that can differentiate into functional heart muscle cells

opens up a new perspective in the long term therapy of heart diseases and reinforces the need to understand the process of normal cardiac development. For similar reasons we study pronephros development in *Xenopus*. The pronephros represents the functional embryonic kidney in this species.

Another focus of the institute is to uncover cellular and molecular mechanisms underlying the elevated regenerative capacity of lower vertebrates. In contrast to mammals, fish and many amphibians can completely restore many internal organs and their appendages after injury. A detailed understanding of the mechanisms regulating this naturally occurring regeneration will aid in the development of regenerative therapies in humans. In the Weidinger lab we study heart and appendage regeneration in the zebrafish model. We focus on the role of extracellular signaling pathways, use systems biology approaches to uncover regulatory networks controlling regeneration and study the mechanisms inducing cellular plasticity during regeneration.

We also study molecular changes underlying the aging process using intestinal stem cells in *Drosophila* (Pandur lab) and hematopoetic stem cells in the mouse (Kühl lab) as model systems. Finally, the molecular design and the regulation of the Wnt signaling network, which controls many essential cellular processes during development, tissue homeostasis and regeneration, is analyzed by the Kühl and Weidinger labs. We use a combination of signaling assays in fish and frog embryos and cultured cells, biochemical approaches and mathematical modeling to uncover novel molecular regulators of this important signaling network. One important approach has been to use quantitative models based on ordinary differential equations and qualitative models in collaboration with bioinformaticians.



The image shows cells of the *Drosophila* midgut. Intestinal stem cells are positive for the GFP-reporter and the Notch ligand Delta (red).

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Selected Publications:

- *Özan G, Sezgin E, Wehner D, Pfister AS, Kühl SJ, Kagermeier-Schenk B, Kühl M, Schwille P and Weidinger G (2013) Lypd6 enhances Wnt/b-catenin signaling by promoting Lrp6 phosphorylation in raft plasma membrane domains, Dev. Cell, 26: 331-45.*
- *Burkhalter MD, Fralish GB, Premont RT, Caron MG and Philipp M (2013) Grk5l controls heart development by limiting mTOR signaling during symmetry breaking, Cell Reports, 4: 625-32.*
- *Herrmann F, Groß A, Zhou D, Kestler HA, Kühl M (2012) A boolean model of the cardiac regulatory network determining first and second heart field identity, PLoS One, 7: e46798.*
- *Tauc HM, Mann T, Werner K, Pandur P (2012) A role for Drosophila Wnt-4 in heart development, Genesis 50: 466-81.*
- *Bugner V, Tecza A, Gessert S, Kühl M (2011) Peter Pan functions independent of its role in ribosome biogenesis during early eye and craniofacial cartilage development in Xenopus laevis, Development, 138: 2369-78.*



Institute of General Medicine

Head of Institute: Prof. Dr. Hans-Peter Zeitler
Keywords: general medicine | prevention | health support

The Institute of General Medicine regards itself as a link between clinical medicine and general medical practice activity.

Our team consists of a secretary, two full-time scientific employees, three part-time employees, 14 general practitioners employed as lecturers, and the director, who is also employed part-time while working for the remainder of his time in his own practice as a GP.

Demographic development has caused an increase in chronically ill and multi-morbid patients. The simultaneous shortage of young GP's necessitates high-quality basic support offered by qualified and motivated family doctors. To do justice to this challenge we offer a family doctor tracking program in the first semester, whereby students are taught by an experienced GP as their tutor about the whole spectrum of their studies to define the reality of work and supply in General Medicine. Within the clinical semesters there is a course in General Medicine consisting of theme-based seminars and lectures in which examples of all important aspects of primary care activity are treated. In addition, there is a two-week traineeship in one of our teaching surgeries, in which the students can become familiar with various interesting features of General Medicine at first hand. Four months of the practical year (PJ) can thus be omitted.

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Another focus of our teaching is prevention and health support. This course is conducted in collaboration with the Section of Sport and Rehabilitation Medicine. In addition to cross-institutional seminars and lectures, this course deals with structured theory as well as practical components, in which students can gain experience in applying prevention in different modules. To respond to this enormous challenge to both teaching and research within such a small department, we work together with more than 150 teaching and research practices.

The main emphasis of our research centers particularly on the study of the reality of supply and the decision-making processes in General Medicine. In addition to this, we are currently working on a project sponsored by the BMG to define ways of diagnosing rare illnesses within the context of primary health care.



Selected Publications:

- *Gröber-Grätz D, Waldmann U-M, Knaus W, Gulich M, Zeitler H-P (2012): Der Einfluss des Beipackzettels auf die medikamentöse Adhärenz bei hausärztlichen Patienten Dtsch. Med. Wochenschrift 137(27):1395-400.*
- *Gröber-Grätz D, Gulich M, Zeitler H-P (2011): Überweisungspraxis zwischen niedergelassenen Allgemeinärzten und Spezialisten in Baden-Würrtemberg vor einführung der Hausarztverträge Z Allg Med 2011(10) 415-421.*
- *Gröber-Grätz D, Gulich M (2011): Impact of drugs disount contracts on pharmacies and on patient´s drug supply Journal of Public Health 2010; 18(6): 583-589.*



The faculty at work.

Institute of the History, Philosophy and Ethics of Medicine

Acting Director of the Institute: PD Dr. Igor Polianski
Keywords: Clinical ethics | history of medicine | medical ethics | philosophy of medicine

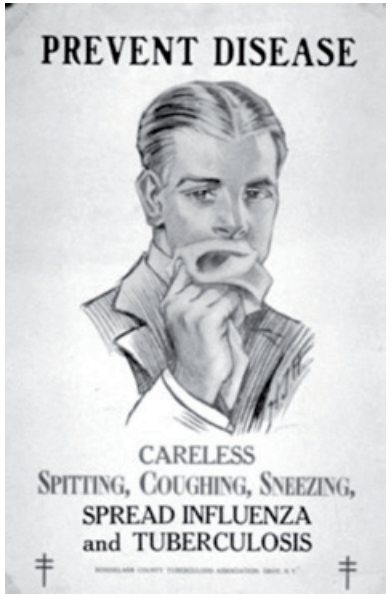
Our institute is dedicated to research and education covering a wide spectrum of medical theory and practice: The history and ethics of medicine in addition to medical theory and the philosophy of science are topics that are vital for medical practitioners and the researchers of tomorrow. Furthermore, the institute coordinates and conducts a counseling service to tackle ethical questions in the fields of medicine and health care at the University Hospital.

The institute connects the history of medicine and the life sciences to modern dilemmas concerning philosophy, medical ethics and medical sociology. By exploring the social and cultural dimensions of medicine, this helps to bridge the gap between biomedical research, clinical practice and social issues as reflected in the humanities and social sciences. With a faculty covering various scientific backgrounds – medicine and the life sciences, cultural and historical anthropology, philosophy, political studies, history and sociology of science – the institute practices a truly transdisciplinary approach.

At the institute, medical students and students of molecular medicine are taught the historical, philosophical and ethical backgrounds of their field to enable them to cope adequately with the challenges of their later everyday professional life. Furthermore, the institute presents on-the-job training for physicians, nurses and other hospital staff.

Research at the institute includes a great variety of methods and topics such as international comparative studies in the history of medicine and biology, the origins of biomedicine, and the philosophy of science and medicine, while placing a special focus on medical ethics. Current projects include the shaping of medicine as a life science since the year 1900, the transfer of medical knowledge and scientific networks, classification and evolution in medical diagnostics and medical imaging, the ethics of stem cell research, and the development of clinical ethics from an intercultural perspective.

The institute also coordinates the University's Center of Medicine and Society. In the field of biomedical sciences, responsible future-oriented research will only happen by means of dialogue with contemporary society and by considering the basic historical, theoretical and ethical principles of medical research and action. In this respect, the center intends to offer an interdisciplinary and multiperspective approach. To achieve this, Ulm University with its record of intensive research provides the perfect setting and conditions. The Center of Medicine and Society is able to act as a showcase for biomedicine and the humanities, which deal with medical issues, and also serves as a platform for the life sciences by reflecting upon its own actions. The institute offers its expertise in the arts and humanities as well as the social sciences to act as an interpreter and promoter of interdisciplinary medical research.



Public health poster from Spanish flu era, ca. 1918,
Poster by Rensselaer County (New York) Tuberculosis Association.
The figure shows a classical example of material that requires analysis from a cultural perspective. The understanding of current scientific discourses and public fears about the pandemics of today and tomorrow demand an analytical approach and the background of the history of medical knowledge and medical ethics.

The institute has established a reference library which houses a constantly expanding collection of specialized books and research literature.
In addition, current journals on the history, philosophy and ethics of medicine are also available. The entire collection is listed in the online catalog of the University Library. Moreover, there is an index of newspaper articles concerning numerous scientific issues on the history, philosophy and ethics of medicine.

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Selected Publications:

- *Fangerau H, Polianski I (Hrsg.) (2011): Medizin im Spiegel ihrer Geschichte, Theorie und Ethik. Schlüsselthemen für ein junges Querschnittsfach, Steiner, Stuttgart.*
- *Polianski I, Fangerau H (2012): "Toward "Harder" Medical Humanities: Moving Beyond the "Two Cultures" Dichotomy", Academic Medicine 87 (1): 121-126.*
- *Imhof C, Badura-Lotter G (2012) Trauer und Ohnmacht – Effekte emotionaler Betroffenheit auf die Praxis der Ethikberatung in der Pädiatrie. Jahrbuch Ethik in der Klinik (5) 283-287.*
- *Fangerau H, Geisler H, Halling T, Martin W (Hrsg.) (2013): Classification and Evolution in Biology, Linguistics and the History of Science. Concepts, Methods, Visualization, Steiner, Stuttgart.*
- *Lenk C, Duttge G, Fangerau H (2014): Handbuch Ethik und Recht der Forschung am Menschen, Springer, Heidelberg et al.*



A new study participant is included in the Ulmer SPATZ Gesundheitsstudie and welcomed by the study team.

Institute of Epidemiology and Medical Biometry

Head of Institute: Prof. Dr. Dietrich Rothenbacher, MPH

Keywords: cardiometabolic diseases | asthma and allergies | health in older adults | data management | statistical methodology

Since December 2010 the Institute of Epidemiology and the Institute of Medical Biometry have been combined. Thus, the expertise for the planning, conduct and analysis of population-based and clinical epidemiological studies, registries and randomized clinical studies is now concentrated in the institute.

The research profile includes asthma and allergic diseases as well as cardiovascular disease, metabolic disorders and cancer. Several large population-based studies are conducted as collaborative research projects. In 2012 a birth cohort study that includes over 1,000 families was

established (Ulmer SPATZ Gesundheitsstudie). Furthermore, the institute is the data center for many multi-center studies (e.g. ISAAC Phase II, GABRIEL) as well as for the prevention program for school-children “The Healthy Boat.”

The institute is also hosting several registries. In cooperation with the Department of Neurology the first clinical epidemiological register for amyotrophic lateral sclerosis (ALS) in Germany was implemented as well as several RCT’s. In addition, data from the international Huntington-registry EHDN are analyzed. Interdisciplinary geriatric research has also been successfully established at the institute (ActiFE-study).

Furthermore, the DPV (diabetes patient documentation), an electronic data-based documentation software for all forms of diabetes in both children and adults, is operated here (Prof. Holl). Moreover, research on statistical methodology in clinical studies is also conducted (Prof. Muche).
The institute teaches students from several study programs and clinical researchers in epidemiology and biometry by means of lectures, seminars and a consultation service. In addition, an annual International Summer School of Epidemiology has been held for the past 25 years in cooperation with the Gillings School of Global Public Health at the University of North Carolina (UNC) in Chapel Hill (USA).



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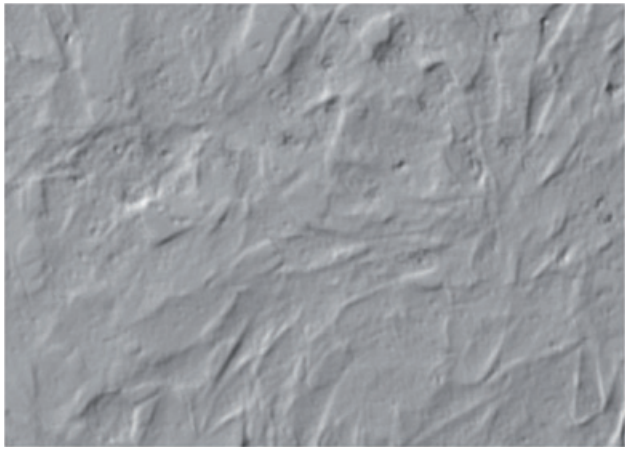
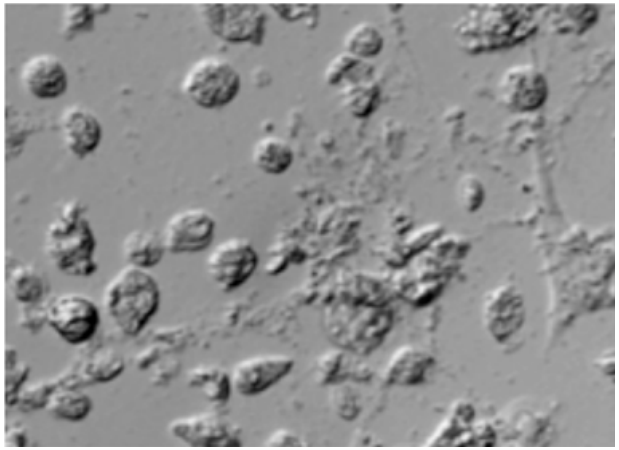
Selected Publications:

- *Shlipak MG, Matsushita K, Ärnlöv J, Inker LA, Katz R, Polkinghorne K, Rothenbacher D, Sarnak MJ, Astor BC, Coresh J, Levey AS, Gansevoort RT, for the CKD Prognosis Consortium. Cystatin C versus creatinine in determining risk based kidney function. N Engl J Med 2013; 369:932-43.*
- *Nagel G, Weinmayr G, Flohr C, Kleiner A, Strachan DP; ISAAC Phase Two Study Group. Association of pertussis and measles infections and immunizations with asthma and allergic sensitization in ISAAC Phase Two. Pediatr Allergy Immunol 2012;23:737-46.*
- *Rosenbauer J, Dost A, Karges B, Hungele A, Stahl A, Bächle C, Gerstl EM, Kastendieck C, Hofer SE, Holl RW on behalf of the DPV Initiative and the German BMBF Competence Network Diabetes mellitus. Improved metabolic control in children and adolescents with type 1 diabetes – a trend analysis using prospective multi-center data from Germany and Austria. Diabet Care 2012; 35, 80 – 86.*
- *Mayer B, Muche R. Chances and obstacles of pilot projects in animal research for statistical sample size calculation. Int J Biol Med Res. 2012; 3: 2319-2323*
- *Ege MJ, Mayer M, Normand AC, Genuneit J, Cookson WO, Braun-Fahrländer C, Heederik D, Piarroux R, von Mutius E; GABRIELA Transregio 22 Study Group. Exposure to environmental microorganisms and childhood asthma. N Engl J Med 2011; 364:701-9.*



Conventional chemotherapeutic drugs failed to kill chemoresistant glioblastoma cells.



D,L-Methadone sensitized glioblastoma cells for conventional chemotherapeutic drug treatment.

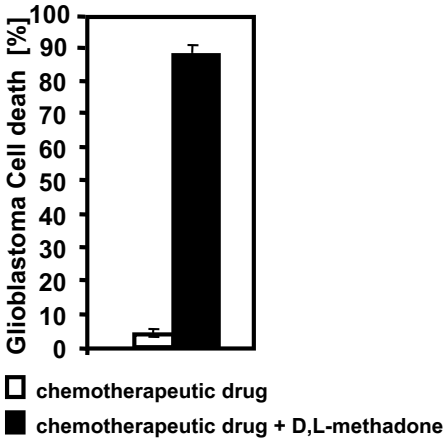
Institute of Forensic Medicine

Head of Institute: Prof. Dr. Erich Miltner

Keywords: D,L-Methadone | apoptosis | cancer | DNA-methylation | medical law

The Institute of Forensic Medicine has 35 employees and concentrates on three fields of work to perform all routine services: forensic medicine; forensic toxicology; and forensic genetics. Distinctive features include: the performance of CT-scans with scanner adjacent before routine autopsies; services in the DNA laboratory for DNA profiling of single skin scales after microscopical selection; heteroplasmy evaluation in mitochondrial DNA control region using pyrosequencing; and analysis of DNA-methylation in different human tumor tissues. Additionally, we conduct scientific work in medical law. In the molecular research laboratory, we focus on oncology in such areas as apoptosis, DNA-damage and cell cycle signaling of anticancer drugs, radiation and opioids, and the

development of new strategies for cancer treatment. We have discovered that D,L-methadone, which is commonly used to break addictions to opioid drugs, has the surprising power to kill and to sensitize for conventional therapies leukemia cells and solid tumors, including those in the treatment of resistant forms of cancer. This finding provides the basis for developing new strategies to establish D,L-methadone as an additional therapeutic anticancer drug and also for further investigations to combine D,L-methadone with chemotherapy or radiation to overcome chemo- and radioresistance in cancer in order to improve therapeutic success.



D,L-Methadone increased effectiveness of chemotherapeutic drugs in killing cancer cells.

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Selected Publications:

- *Friesen C, Hormann I, Roscher M, Fichtner I, Alt A, Hilger RA, Debatin KM, Miltner E. Opioid receptor activation triggering downregulation of cAMP improves effectiveness of anti-cancer drugs in treatment of glioblastoma. Cell Cycle 2014, 13: 1560-1570.*
- *Friesen C, Roscher M, Hormann I, Fichtner I, Alt A, Hilger RA, Debatin KM, Miltner E. Cell death sensitization of leukemia cells by opioid receptor activation. Oncotarget 2013, 4: 677-690.*
- *Friesen C, Roscher M, Hormann I, Leib O, Marx S, Moreno J, Miltner E. Anti-CD33-antibodies labelled with the alpha-emitter Bismuth-213 kill CD33-positive acute myeloid leukaemia cells specifically by activation of caspases and break radio- and chemoresistance by inhibition of the anti-apoptotic proteins X-linked inhibitor of apoptosis protein and B-cell lymphoma-extra large. European Journal of Cancer 2013, 49: 2542-2554.*
- *Winkler M, Skopp G, Alt A, Miltner E, Jochum Th, Daenhardt C, Sporkert F, Gnann H, Weinmann W, Thierauf A. Comparison of direct and indirect alcohol markers with PEth in blood and urine in alcohol dependent inpatients during detoxication. Int J Legal Med, 2013; 127 (4): 761-768.*
- *Pfeifer CM, Klein-Unseld R, Klintschar M, Wiegand P. Comparison of different interpretation strategies for low template DNA mixtures. Forensic Sci Int Genet 2012, 6 (6): 716-22.*



Medical student St. Weissinger together with PD Dr. J. Lennerz at the laser dissection microscope, a device that enables the isolation of single neoplastic cells out of a tissue section. These captured cells are then further processed, e.g. by PCR, to obtain mRNA and/or DNA for detailed analysis of transcripts or target genes.

Institute of Pathology

Head of Institute: Prof. Dr. Peter Möller

Keywords: Lymphoma research | Sarcoma research | Biomarkers in oncology | Dementia research | Diagnostic oncology

Profile of the Institute/Department (1.500 characters including spaces):
The Institute of Pathology is an integral part of the Medical Faculty of Ulm University and of the Comprehensive Cancer Center Ulm (CCCU). The institute runs four diagnostic laboratories, one of which comprises an accredited facility for diagnostic molecular pathology that is especially engaged in molecular oncology. The institute employs 63 personnel, most of whom are female and among whom five are board-certified pathologists and two are neuropathologists. We have four positions for medical residents in training. Further academics include two geneticists and one molecular biologist/biochemist. Currently, the department hosts two medical students working on their MD thesis and one of these recently received the *Württembergischer Krebspreis* (Württemberg Cancer Award) for young scientists.

The institute is primarily engaged in clinical and surgical pathology covering all disciplines of Ulm University Medical Center and smaller surrounding hospitals. The number of diagnosed patients amounts to more than 40,000 per year. The pathologists with board certificates are constitutive members of the weekly interdisciplinary tumor boards of the CCCU, of surrounding hospitals and those of the national Bone Tumor Working Group.

The head of the institute is one of six members of a panel of German reference pathologists specializing in lymph node and lymphoma pathology. This panel conducts reference pathology for clinical trials in childhood and adult Hodgkin and non-Hodgkin lymphoma and is engaged in trial-associated pathological and clinical research in lymphoma. The head was among the first to describe



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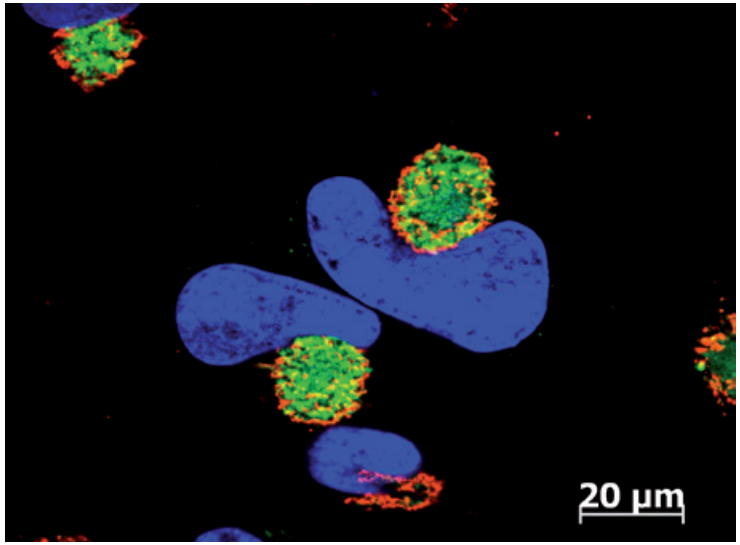
mediastinal large B cell lymphoma. Other scientific topics of the institute include the generation and molecular and genetic characterization of novel cancer cell lines derived from a variety of cancers and the molecular characterization of tumor entities like leiomyosarcoma, liposarcoma and chordoma. Moreover, we are interested in the analyses of therapy-resistant prostate carcinoma. In clinical research, the focus is on the detection of prognostic biomarkers. The institute and the CCCU, together with its affiliated biobank, have cohorts of patients and their freshly frozen and paraffin-embedded tumor tissues for the following disease entities: classical Hodgkin lymphoma; gastric lymphoma; pancreatic ductal adenocarcinoma; leiomyosarcoma; and chordoma with clinical follow-up data spanning up to more than a decade.

The institute has a separate division of neuropathology that is headed by Prof. Dr. Dietmar Thal. His research focuses on Alzheimer's disease and other related neurodegenerative disorders. This group introduced a staging system ("Thal phases") for amyloid plaque pathology that has been incorporated into the current guidelines for the neuropathological diagnosis of Alzheimer's disease by the National Institute of Aging and the Alzheimer's Association. Current research projects focus on the discovery of Alzheimer's disease initiation and propagation mechanisms and their relevance for therapeutic approaches.

Selected Publications:

- *Schif B, Lennerz JK, Kohler CW, Bentink S, Kreuz M, Melzner I, Ritz O, Trümper L, Loeffler M, Spang R, Möller P. (2013): SOCS1 mutation subtypes predict divergent outcomes in diffuse large B-Cell lymphoma (DLBCL) patients. Oncotarget. 4(1): 35-47.*
- *Ritz O, Rommel K, Dorsch K, Kelsch E, Melzner J, Buck M, Leroy K, Papadopoulou V, Wagner S, Marienfeld R, Brüderlein S, Lennerz JK, Möller P. (2013): STAT6-mediated BCL6 repression in primary mediastinal B-cell lymphoma (PMBL). Oncotarget. 4(7): 1093-102.*
- *Flossbach L, Holzmann K, Mattfeldt T, Buck M, Lanz K, Held M, Möller P, Barth TF. (2013): High-resolution genomic profiling reveals clonal evolution and competition in gastrointestinal marginal zone B-cell lymphoma and its large cell variant. Int J Cancer. 132(3): E116-27.*
- *Schmid SJ, Glatzel MC, Welke C, Kornmann M, Kleger A, Barth TF, Fulda S, Lennerz JK, Möller P. (2013): Absence of FLICE-inhibitory protein is a novel independent prognostic marker for very short survival in pancreatic ductal adenocarcinoma. Pancreas. 42(7): 1114-9.*
- *Hyman, B.T.; Phelps, C.H.; Beach, T.G.; Bigio, E.H.; Cairns, N.J.; Carrillo, M.C.; Dickson, D.W.; Duyckaerts, C.; Frosch, M.P.; Masliah, E.; Mirra, S.S.; Nelson, P.T.; Schneider, J.A.; Thal, D.R.; Thies, B.; Trojanowski, J.Q.; Vinters, H.V.; Montine, T.J. National Institute on Aging–Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. Alzheimer Dementia 8 (2012) 1-13.*



Colored viruses:
Localization of cytomegaloviruses (green) and a cellular protein (red) near the cell nucleus (blue).

Institute of Virology

Head of Institute: Prof. Dr. Thomas Mertens

Keywords: Diagnostic | Cytomegalovirus | Therapy | Resistance | Pathogenesis-Morphogenesis

The institute performs virological diagnostics for Ulm University Hospital as well as for some external senders. For the most part, these are highly specialized laboratory services based on specifically established and validated methods. One main focus is the monitoring of immunosuppressed patients, especially bone marrow transplant recipients in pediatric and adult medicine. This monitoring is decisive for the outcome of highly specialized therapies since these patients are often vitally threatened by exogenous and reactivated viral infections. Other foci are the diagnosis of respiratory infections as well as virus infections during pregnancy.

Research is focused on Human Cytomegalovirus (HCMV), a member of the herpes virus family. Teaching is provided for students studying human medicine, dentistry, biology and informatics as well as for bachelor and master students of courses in Molecular Medicine and students of the International Graduate School in Molecular Medicine.

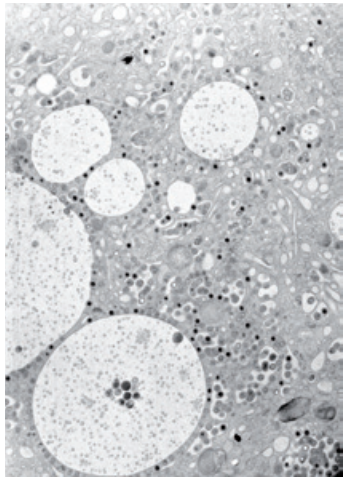
In addition to two permanent professorships, the institute consists of six assistants and eight medical technicians. The majority of these work in the diagnostic section.

For many years, a close cooperation has been established with the universities of Padua and Bologna. Thus, there are always a number PhD students from Italy (see picture) as well as qualified PhDs working at the institute. With regards to research on CMV, there are various work groups focused on such topics as the mechanisms of HCMV resistance against existing antiviral substances. This work resulted in essential findings concerning CMV-coded proteins that have since been published in high ranking journals. Methods and procedures have been established and, at the end of 2009, a database was released enabling interested researchers using the worldwide web to correlate mutations in CMV genomes that confer resistance to corresponding resistance phenotypes. We have noticed that this website has been used extensively in recent months.

The director of the institute is the head of a network of the Robert Koch Institute focused on infections during pregnancy and immune suppression. This institute is a national reference laboratory for human CMV.

Another research group is working on the function of viral tegument proteins for the morphogenesis of CMV. This research was funded by a *Schwerpunktprogramm* (Priority Program) of the *Deutsche Forschungsgemeinschaft* (DFG), the German Research Foundation. This project has resulted in some understanding of the biology of this very complex virus and will also enable the identification of new targets for antiviral intervention. One research project focuses on the effects of CMV infection in monocytes and macrophages. A special aspect of this work is that these cells are central cells of the immune response and are not only infected but are obviously also used as sites of latent CMV infection. In this context, results showed that differentially polarized macrophages vary significantly concerning HCMV infection.

Finally, we are also studying the role of natural killer cells in the control of human cytomegalovirus infections. This research is based on in vitro models and also on materials from pediatric SCID patients.



Virus particles:
Individual viruses can only be visualized by electron microscopy. Multiple cytomegalovirus particles are adjacent to and budding into cellular vesicles.

In the field of CMV research, the modulation of cellular genes by viral gene expression is also examined. This aspect reveals special importance concerning research on human diseases which are not primarily classified as infectious diseases, e.g. atherosclerosis.

Concerning clinical virology, there is close cooperation with various clinical departments and institutes focusing on research dealing with different viral infections.

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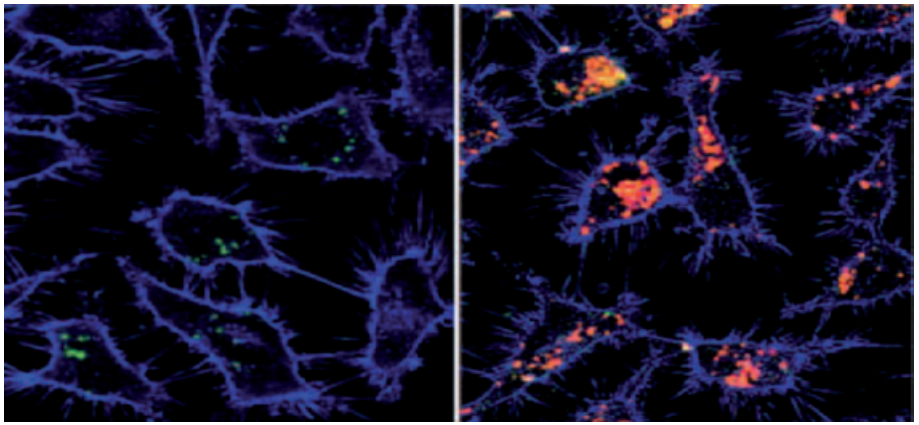
Selected Publications:

- *Wu Z, Sinzger C, Frascaroli G, Reichel J, Bayer C, Wang L, Schirmbeck R, Mertens T. Human cytomegalovirus-induced NKG2C(hi) CD57(hi) natural killer cells are effectors dependent on humoral antiviral immunity. J Virol. 2013 Jul;87(13):7717-25.*
- *Brock I, Krüger M, Mertens T, von Einem J. Nuclear targeting of human cytomegalovirus large tegument protein pUL48 is essential for viral growth. J Virol. 2013 May;87(10):6005-19.*
- *Schauflinger M, Villinger C, Mertens T, Walther P, von Einem J. Analysis of human cytomegalovirus secondary envelopment by advanced electron microscopy. Cell Microbiol. 2013 Feb;15(2):305-14.*
- *Bayer C, Varani S, Wang L, Walther P, Zhou S, Straschewski S, Bachem M, Söderberg-Naucler C, Mertens T, Frascaroli G. Human cytomegalovirus infection of M1 and M2 macrophages triggers inflammation and autologous T-cell proliferation. J Virol. 2013 Jan;87(1):67-79.*
- *Reiser M, Wieland A, Plachter B, Mertens T, Greiner J, Schirmbeck R. The immunodominant CD8 T cell response to the human cytomegalovirus tegument phosphoprotein pp65(495-503) epitope critically depends on CD4 T cell help in vaccinated HLA-A*0201 transgenic mice. J Immunol. 2011 Sep 1;187(5):2172-80.*



Nanofibrils boost retroviral transduction. Analysis of HeLa cells (blue) inoculated with either MLV–YFP (green) alone or in the presence of nanofibrils. Adapted from Yolamanova et al., Nature Nanotechnology 2013.

Institute of Molecular Virology

Head of Institute: Prof. Dr. Frank Kirchhoff

Keywords: Accessory viral proteins | AIDS | HIV | immune evasion | SIV

The Institute of Molecular Virology was established in Spring 2009 and has currently 30 members including five scientists, six research technicians, 13 PhD students, four master students and two secretaries. Two employees come from India and South Africa respectively.

One particular research interest is to determine which factors contribute to the high virulence and effective spread of HIV-1. Four groups of HIV-1 (M, N, O and P) have been described and each one is the result of an independent transmission of a simian immunodeficiency virus (SIV) from apes to humans. We found that better adaptation to a human host may explain why only HIV-1 groups M (major) and O (outlier) have spread significantly in the human population. A deletion in the human version of the restriction factor “tetherin” that inhibits the release of HIV particles confers resistance to the viral Nef protein used by most simian immunodeficiency viruses to antagonize this antiviral factor. Pandemic HIV-1 group M cleared this hurdle by acquiring the ability to utilize the viral protein U (Vpu) to counteract tetherin. In contrast, the Nef proteins of epidemic HIV-1 group O strains evolved to target a region adjacent to this deletion to keep tetherin away from the cell surface. Thus, acquisition of anti-tetherin activity was most likely a prerequisite for the spread of the AIDS pandemic. Furthermore, our results suggest that differences in Nef function help to explain why HIV-1 causes AIDS, whereas monkeys that are naturally infected with SIV do not develop the disease.

Another interest are endogenous factors that modulate viral infections. In cooperative studies, we screened complex peptide libraries from human sources to identify novel inhibitors and enhancers of HIV-1 infection. We identified a naturally occurring HIV-1 entry inhibitor and demonstrated that an optimized derivative thereof is safe and effective against HIV-1 in a first clinical trial. Strikingly, our analyses also showed that semen contains amyloid fibrils that boost HIV-1 infection. Based on this discovery, we developed fibril-forming peptides that improve retroviral gene transfer. Recently, we identified a natural CXCR4 antagonist that not only blocks infection by CXCR4-tropic HIV-1 strains but also promotes the mobilization of stem cells, suppresses the migration of cancer cells and exerts anti-inflammatory effects in mouse models. This CXCR4 antagonist is generated from a highly abundant precursor at sites of infection or inflammation and may thus introduce a new concept in the regulation of the activity of G protein-coupled receptors. Our results show that screening of complex peptide libraries derived from human sources allows the discovery of agents with highly unexpected activities that have implications beyond HIV/AIDS.



Discussion of scientific data

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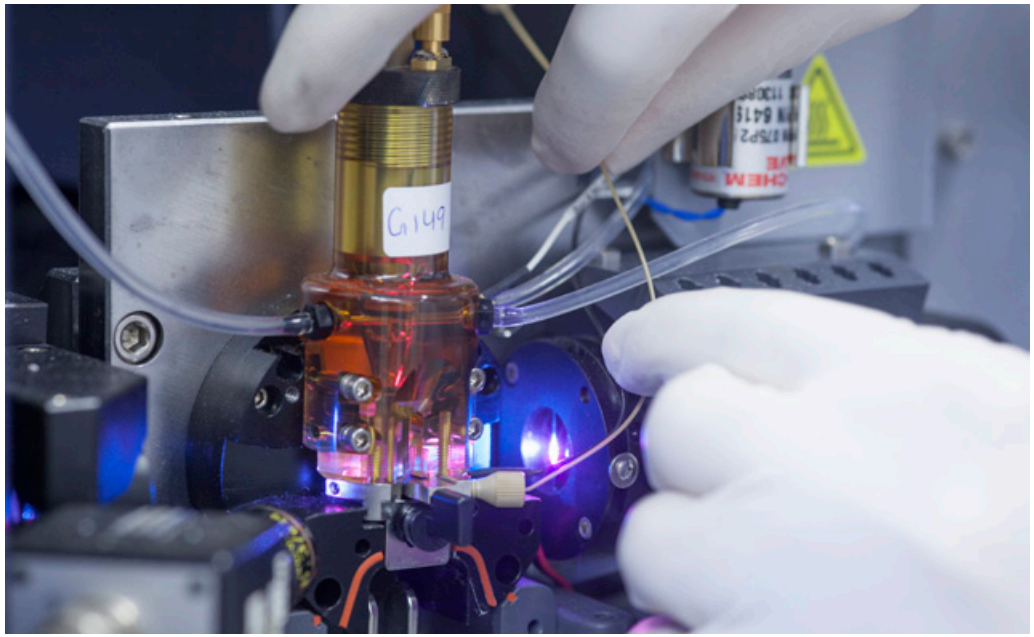
Selected Publications:

- *Usmani SM, Zirafi O, Müller JA, Sandi-Monroy NL, Yadav JK, Meier C, Weil T, Roan NR, Greene WC, Walther P, Nilsson KP, Hammarström P, Wetzel R, Pilcher CD, Gagsteiger F, Fändrich M, Kirchhoff F, Münch J. (2014). Direct visualization of HIV-enhancing endogenous amyloid fibrils in human semen. Nat. Commun. 5:3508.*
- *Yolamanova M, Meier C, Shaytan AK, Vas V, Bertoncini CW, Arnold F, Zirafi O, Usmani SM, Müller JA, Sauter D, Goffinet C, Palesch D, Walther P, Roan NR, Geiger H, Lunov O, Simmet T, Bohne J, Schrezenmeier H, Schwarz K, Ständker L, Forssmann WG, Salvatella X, Khalatur PG, Khokhlov AR, Knowles TP, Weil T, Kirchhoff F, Münch J. (2013). Peptide nanofibrils boost retroviral gene transfer and provide a rapid means for concentrating viruses. Nat. Nanotechnol. 8, 130-6.*
- *Schmökel J, Li H, Shabir A, Yu H, Geyer M, Silvestri G, Sodora DL, Hahn BH, Kirchhoff F. (2013). Link between Primate Lentiviral Coreceptor Usage and Nef Function. Cell Reports 5, 997-1009.*
- *Palesch D, Kirchhoff F. (2013). First steps toward a globally effective HIV/AIDS vaccine. Cell 155, 495-497.*
- *Götz N, Sauter D, Usmani SM, Fritz JV, Goffinet C, Heigele A, Geyer M, Bibollet-Ruche F, Learn GH, Fackler OT, Hahn BH, Kirchhoff F. (2012). Reacquisition of Nef-mediated tetherin antagonism in a single in vivo passage of HIV-1 through its original chimpanzee host. Cell Host Microbe. 12, 373-80.*



Institute of Immunology

Head of Institute: Prof. Dr. Hassan Jumaa

Keywords: Hematopoiesis | Fate Mapping | Signal Transduction | Differentiation | Oncogene

In September 2013, Prof. Jumaa (formerly of the Max-Planck Institute of Immunobiology and Epigenetics, Freiburg) was appointed as the new director of the institute to succeed Prof. Rodewald, who moved to the DKFZ/Heidelberg in 2010, and Prof. Fehling, who served as interim director. The institute currently accommodates two research groups headed by Prof. Jumaa and Prof. Fehling.
A central topic of the Jumaa research group is the characterization of B cell antigen receptor (BCR) signaling in the development and proliferation of normal B cells as compared with transformed cells. In our previous work, we established a unique in vitro experimental system that allows us to dissect the signaling cascades that act downstream of the BCR. Using this system, we also investigate the mechanisms that trigger BCR signaling in B cell lymphomas and may be involved in the pathogenesis of human lymphoproliferative diseases. Moreover, we investigate the oncogenic potential of BCR-associated signaling proteins such as the tyrosine kinase Syk. To this end, we have established animal models for inducible expression of Syk variants that were isolated from human lymphomas.

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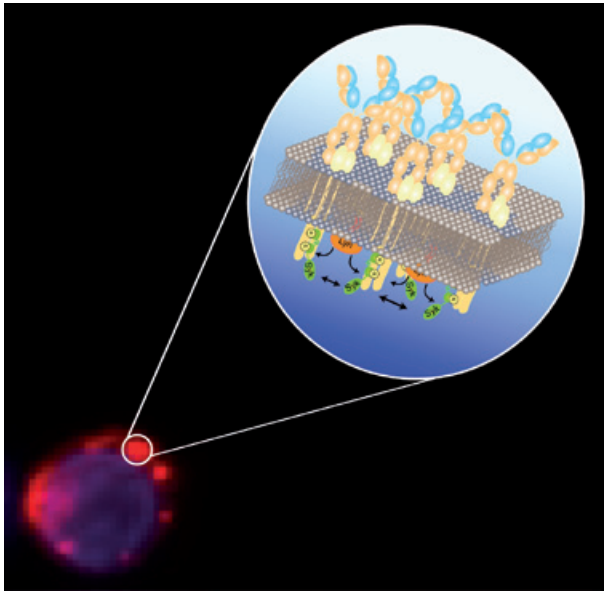
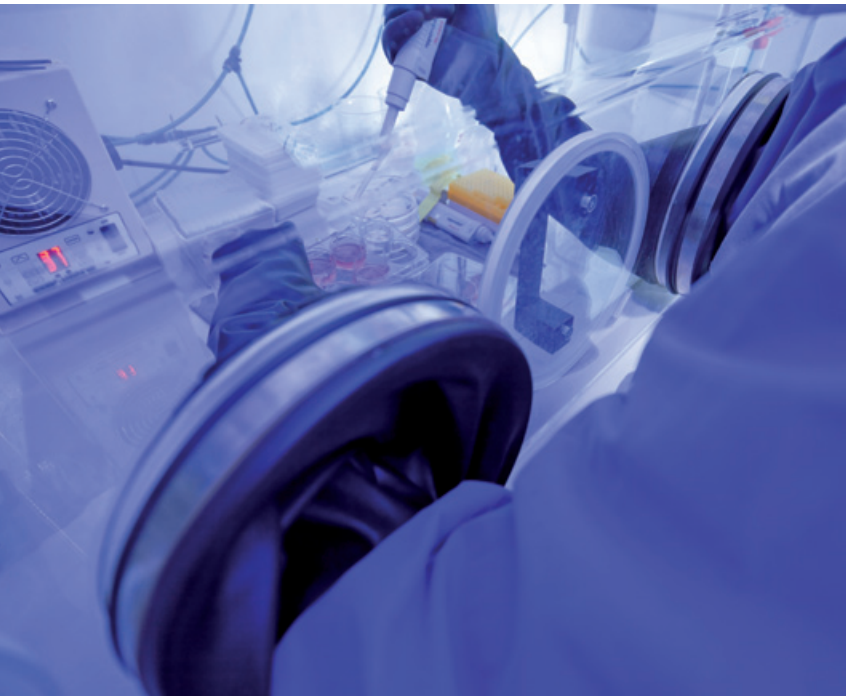
The generation and analysis of genetically modified mouse strains define the prime technical expertise of the Fehling research group. The laboratory currently focuses on two key topics. One set of projects aims at a better molecular understanding of the (patho-) physiological function of "*Mixed-Lineage-Leukemia 5*," a gene encoding an epigenetic regulator and suspected tumor suppressor of human myeloid leukemias. MLL5-deficient mice generated in the laboratory have revealed key roles of this protein in normal hematopoietic stem cell function and may provide a valuable animal model for investigating potential contributions of MLL5 to leukemogenesis. In another line of investigation, the Fehling group has generated several sophisticated "knock-in" mouse strains to directly visualize developmental fate decisions in the hematopoietic system using techniques of in vivo lineage tracing. This project has recently provided important novel insights into early T lymphopoiesis (J.Exp.Med. 2013).



Autonomous clustering of B cell antigen receptors (BCRs) on the surface of Chronic Lymphocytic Leukemia (CLL) cells and a proposed model for BCR organization.

Selected Publications:

- *Luche H, Nageswara Rao T, Kumar S, Tasdogan A, Beckel F, Blum C, Martins VC, Rodewald HR, Fehling HJ. (2013) In vivo fate mapping identifies pre-TCRalpha expression as an intra- and extrathymic, but not pre-thymic, marker of T lymphopoiesis. J Exp Med 210:699-714.*
- *Hug E, Hobeika E, Reth M, Jumaa H. (2014). Inducible expression of hyperactive Syk in B cells activates Blimp-1-dependent terminal differentiation. Oncogene 33:3730-3741*
- *Dühren-von Minden M, Übelhart R, Schneider D, Wossning T, Surova E, Bach M, Hofman D, Köhler F, Wardemann H, Zirlik K, Veelken H, Jumaa H. (2012). Chronic lymphocytic leukemia is driven by antigen-independent cell autonomous signaling. Nature 489:309-312.*
- *Alkhatib A, Werner M, Hug E, Herzog S, Eschbach C, Faraidun F, Köhler F, Jumaa H. (2012). FoxO1 induces Ikaros splicing to promote immunoglobulin gene recombination. J Exp Med 209:395-406.*
- *Teupser D, Weber O, Rao TN, Sass K, Thiery J, Fehling HJ (2011). No reduction of atherosclerosis in C-reactive protein (CRP)-deficient mice. J Biol Chem 286: 6272-6279.*



Institute of Medical Microbiology and Hospital Hygiene

Head of Institute: Prof. Dr. Steffen Stenger

Keywords: Bacterial immune escape mechanisms | disease infection immunology | infection epidemiology | intracellular pathogens | microbial pathogenesis

The Institute of Medical Microbiology and Hospital Hygiene is responsible for the diagnosis of microbial infections in a broad spectrum of clinical samples. Each year about 60,000 materials are investigated for the presence of bacteria, fungi and parasites. In addition to its activities as a clinical diagnostic laboratory, the hospital hygiene section (headed by Prof. Dr. Heike von Baum) is responsible for the hygiene management of the university clinic.

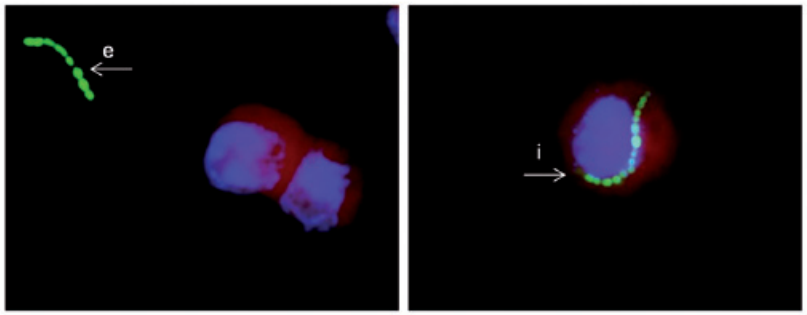
Teaching activities include lectures and practical courses for students of the Medical School, the Dental School, and bachelor and master students of Molecular Medicine. Traditional lectures are supplemented by more interactive teaching in problem-oriented learning (POL) courses and e-learning programs.

The scientific activity of the institute is covered by four independent research groups specializing in various aspects of infectious diseases which entail basic science as well as more clinically-oriented research.

Research Group: Infection Epidemiology

Head: Prof. Dr. Heike von Baum

This group is focusing on infection epidemiology of methicillin resistant *S. aureus* strains (MRSA), pathogens in drinking water and community acquired pneumonia.



Depicted are streptococci (*S. agalactiae*) following incubation with human monocyte-derived cells. Bacteria are fluorescently labeled with EGFP. On the left, bacteria are located extracellularly (e), while on the right, bacteria are found intracellulary (i) in the cytoplasm of the eukaryotic cell.

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Research Group: Chlamydia

Head: Prof. Dr. Andreas Essig

The research activities are centered on the intracellular pathogens *Chlamydia pneumoniae*, *Chlamydia trachomatis* and *Chlamydia abortus*. Current projects of the group are aimed at the identification of antigenic surface structures of chlamydia that could serve as diagnostic markers in serological investigations.

Research Group: Streptococcal Research

Head: Prof. Dr. Barbara Spellerberg

The focus of the streptococcal research group lies in the elucidation of streptococcal virulence factors and immune escape mechanisms. Research topics include the identification of streptococcal virulence determinants and the detailed characterization of host pathogen interactions.

Research Group: MyTB Laboratory

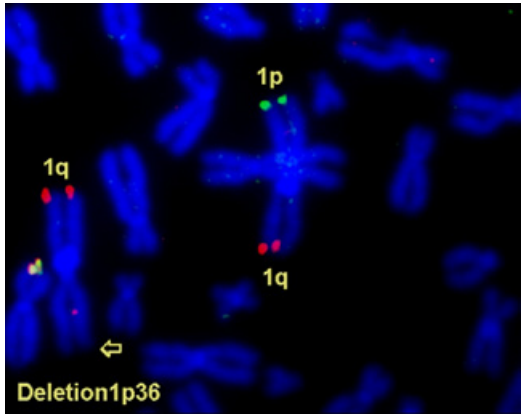
Head: Prof. Dr. Steffen Stenger

This group focuses on the immunological mechanisms directed against mycobacteria. The major goal of the group is the analysis of innate and adaptive effector pathways of the human immune system.

Scientific highlights of our institute in recent years have included the elucidation of molecular host pathogen mechanisms in the interaction of mycobacteria and streptococci with human macrophages. Further research characterized the antibody responses to *Chlamydia abortus* infections and has resulted in an epidemiological study about the outcome of influenza-associated pneumonia.

Selected Publications:

- *von Baum H, Schweiger B, Welte T, Marre R, Suttorp N, Pletz MW, Ewig S; CAPNETZ Study Group. (2011) How deadly is seasonal influenza-associated pneumonia? The German Competence Network for Community-Acquired Pneumonia. Eur Respir J. 37(5):1151-7. doi: 10.1183/09031936.00037410.*
- *Bruns H, Stegelmann F, Fabri M, Döhner K, van Zandbergen G, Wagner M, Skinner M, Modlin RL, Stenger S. (2012) Abelson tyrosine kinase controls phagosomal acidification required for killing of Mycobacterium tuberculosis in human macrophages. J Immunol. 189, 4069-78.*
- *Forsbach-Birk V, Foddis C, Simnacher U, Wilkat M, Longbottom D, Walder G, Benesch C, Ganter M, Sachse K, Essig A. (2013) Profiling antibody responses to infections by Chlamydia abortus enables identification of potential virulence factors and candidates for serodiagnosis. PLoS One. 15;8 e80310. doi: 10.1371/journal.pone.0080310.*
- *Nickel D, Busch M, Mayer D, Hagemann B, Knoll V, Stenger S. (2012) Hypoxia triggers the expression of human β defensin 2 and antimicrobial activity against Mycobacterium tuberculosis in human macrophages. J Immunol. 188, 4001-7.*
- *Sagar A, Klemm C, Hartjes L, Mauerer S, van Zandbergen G, Spellerberg B. (2013)The β-hemolysin and intracellular survival of Streptococcus agalactiae in human macrophages. PLoS One. 4;8e60160. doi: 10.1371/journal.pone.0060160.*



Fluorescence in situ hybridization (FISH) on human metaphase chromosomes showing a 1p36 deletion (absence of green signal on the short arm of one chromosome 1 homolog).

Institute of Human Genetics

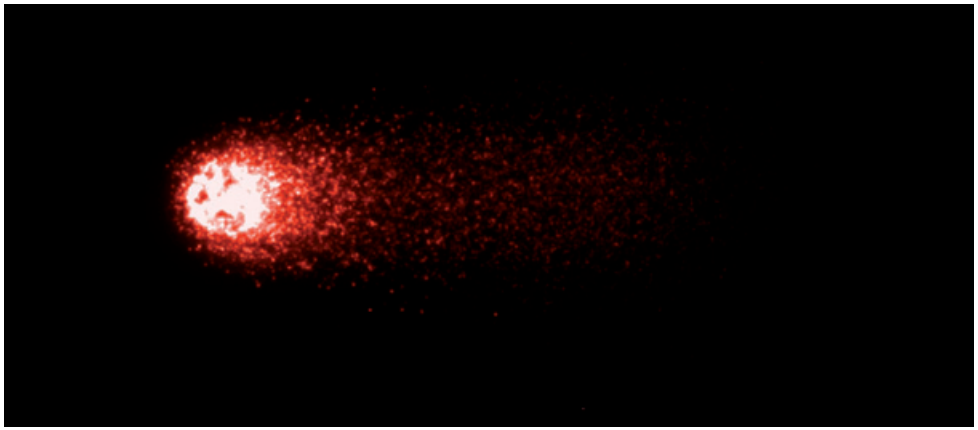
Acting Director of the Institute: Dr. Guntram Borck

Keywords: Molecular genetics | clinical genetics | disease gene identification | genetic epidemiology | DNA repair

The Institute of Human Genetics offers diagnostic genetic analyses as well as genetic counseling for patients and their relatives. The research teams working at the institute are investigating different research topics including the analysis of the causes of complex and monogenic disorders, the mutational mechanisms underlying human genomic rearrangements as well as the mechanisms of mutagen-induced DNA damage and its repair.

The diagnostic laboratory at the institute is state-certified and performs prenatal and postnatal chromosome analysis including G-banded karyotyping and fluorescence in situ hybridization (FISH). Furthermore, molecular genetic testing is performed for approximately 60 genes with a focus on neurogenetic diseases and hereditary cancer predisposition by means of DNA sequence analysis, multiplex ligation-dependent probe amplification (MLPA) and Southern blotting. A next generation sequencing (NGS) platform will be implemented in routine diagnostics in 2014. Genetic counseling is offered in our outpatient clinics by medical geneticists. Moreover, a genetic consultation service is provided for other clinical departments of the University Hospital, e.g. the Children's Hospital and the Department of Neurology. We also collaborate with the Department of Obstetrics and Gynecology in the areas of hereditary breast and ovarian cancer and prenatal diagnosis.

The Institute provides comprehensive teaching of the basics of molecular and clinical genetics for students of medicine, molecular medicine, and biology. By means of lectures, interactive seminars and practical courses performed at the Institute we aim to convey the knowledge



The picture shows a human cell in the comet assay. Induced DNA damage leads to migration of DNA out of the nucleus and to the formation of a “comet” consisting of a head (nucleus) and a tail (DNA that has migrated out of the nucleus). The amount of tail DNA is proportional to the DNA damage.

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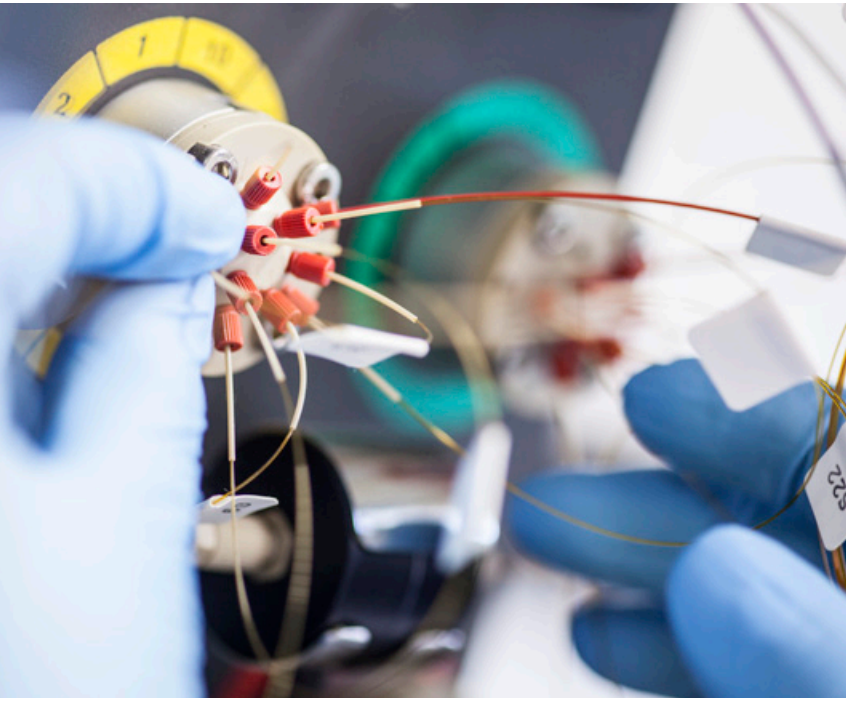
of modern medical and molecular genetics to our students in a vivid manner. We are part of the International Graduate School in Molecular Medicine Ulm and offer MD and PhD projects as well as specializations in genetic diagnostics and clinical genetics for scientists and medical doctors.

Basic and applied genetic research is performed by five independent research teams working on different topics that are important in human and medical genetics. These research topics include: (i) disease gene identification in monogenic and complex genetic human diseases by genome-wide approaches including linkage analysis and exome sequencing; (ii) analysis of DNA damage and DNA repair induced by environmental mutagens using genotoxicity tests such as the comet assay and the micronucleus test and gene expression profiling; (iii) mechanisms underlying large genomic rearrangements including microdeletion and microduplication syndromes using neurofibromatosis as a model disease, (iv) genetic epidemiology and cancer genetics; (v) molecular mechanisms of genomic variation, in particular, structural variation which predisposes to human disease. All research groups are continuously funded by national and international funding agencies and publish their results in internationally renowned and peer-reviewed scientific journals attesting to the quality of their research projects.

Selected Publications:

- *Anttila V, Winsvold BS, Todt U, Borck G, Kubisch C, et al. (2013) Genome-wide meta-analysis identifies new susceptibility loci for migraine. Nature Genet, 5:912-917.*
- *Eeles RA, Olama AA, Maier C, Vogel W, Rinckleb AE, et al. (2013) Identification of 23 new prostate cancer susceptibility loci using the iCOGS custom genotyping array. Nature Genet, 45:385-391.*
- *Kuehner S, Holzmann K, Speit G (2013) Characterization of formaldehyde’s genotoxic mode of action by gene expression analysis in TK6 cells. Arch Toxicol, 87:1999-2012.*
- *Vogt J, Mussotter T, Bengesser K, Claes K, Högel J, Chuzhanova N, Fu C, van den Ende J, Mautner VF, Cooper DN, Messiaen L, Kehrer-Sawatzki H (2012) Identification of recurrent type-2 NF1 microdeletions reveals a mitotic nonallelic homologous recombination hotspot underlying a human genomic disorder. Hum Mutat, 33:1599-1609.*
- *Borck G, Shin BS, Stiller B, Kubisch C, Basel-Vanagaite L. (2012) eIF2γ mutation that disrupts eIF2 complex integrity links intellectual disability to impaired translation initiation. Mol Cell, 48:641-646.*



Institute of Pharmacology and Toxicology

Head of Institute: Prof. Dr. Peter Gierschik

Keywords: Bacterial protein toxins | chemokine receptors | GTP-binding proteins | Rho GTPases | Phospholipases C | Signal transduction

Our primary and long-term mission is to advance the field of Molecular and Cellular Pharmacology and Toxicology in research, teaching and application. Our research efforts are directed at addressing fundamental scientific questions by conducting basic research and at translating basic research findings into sustainable health care improvements by cooperating with the pharmaceutical industry. Our research focus is centered on exploring the transfer of extracellular information of both abstract and concrete essence across the cell membrane. According to the broad and deep impact of pharmacology and toxicology in medicine and the life sciences, the scope of our teaching activities is wide and multidisciplinary, and ranges from medicine, dentistry and molecular medicine to biology, biochemistry, chemistry and pharmaceutical biotechnology. Teaching is conducted at under- and postgraduate levels and in collaboration with the pharmaceutical industry on such topics as national and international (EU) principles of new drug development, registration, and post-marketing risk assessment.

Several research groups are concerned with the role of signal-tranducing GTP-binding proteins (both heterotrimeric G proteins, small GTPases of the Ras superfamily) as well as their cell surface receptors, intracellular regulatory proteins and effectors in cellular signal transduction. Among the G-protein-coupled-receptors, PD Dr. Barbara Moepps is particularly interested in chemokine receptors, which play pivotal and indispensable roles in health and disease by controlling multiple aspects of many cell and tissue functions. Among the small GTPases and intracellular effector proteins, the focus is on Rho GTPases and inositol-phospholipid-specific phospholipases C (PLCs), respectively. In collaboration with other research groups we have determined the three-dimensional



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structure and characterized the functional properties of the heterodimeric complexes between certain Rac GTPases with their regulatory and effector proteins, such as PLCγ2. The latter interaction has recently been shown by the group of Dr. Claudia Walliser to be involved in the development of tumor cell resistance to targeted small molecule therapy.

The institute's research group devoted to toxicological research and health concerns is headed by Prof. Holger Barth and uses biochemical, molecular pharmacological, and cell biological methods to characterize the molecular mechanisms of action of bacterial protein toxins, including diphtheria, pertussis, anthrax, and clostridial toxins. The specific interest is in the transfer of these toxins across cell membranes and their refolding into active biomolecules inside the cell. In collaboration with other research groups, novel pharmacological inhibitors of toxin transport across cell membranes were identified and characterized. It is expected that these findings will not only contribute broadly to our understanding of the impact of these toxins as virulence factors, but will also provide new avenues for the drug therapy of bacterial infections.

Selected Publications:

- *Fahrer J, Schweitzer B, Fiedler K, Langer T, Gierschik P, Barth H (2013): C2-streptavidin mediates the delivery of biotin-conjugated tumor suppressor protein p53 into tumor cells. Bioconjugate Chem. 24: 595-603.*
- *Koenig, C, Fischer-Posovszky P, Rojewski MT, Tews D, Schrezenmeier H, Wabitsch M, Gierschik P, Moepps, B (2013): Absence of CC chemokine receptors CCR2a and CCR2b from human adipose lineage cells. Mol. Cell. Endocrinol. 369: 72-85.*
- *Lang AE§, Ernst K§, Lee H§, Papatheodorou P, Schwan C, Barth H*, Aktories K* (2014): The chaperone Hsp90 and PPIases of the cyclophilin and FKBP families facilitate membrane translocation of Photorhabdus luminescens ADP-ribosyltransferases. Cell. Microbiol. 16:490-503.*
- *Ng D§, Fahrer J§, Eisele K, Ling Kuan S, Lamla M, Barth H*, Weil T* (2013): Efficient delivery of p53 and cytochrome C by supramolecular assembly of a dendritic multi-domain delivery system. Adv. Healthcare Mater. 2:1620-1629 (§contributed equally; *corresponding authors).*
- *Pfreimer M, Vatter P, Langer T, Wieland T, Gierschik P, Moepps B. (2012): LARG links histamine-H1-receptor-activated Gq to Rho-GTPase-dependent signaling pathways. Cell. Signal. 24:652-663.*



Institute of Naturopathic Medicine and Clinical Pharmacology

Head of Institute: Prof. Dr. Thomas Simmet
Keywords: Chemistry of natural products | nanomaterials | immunopharmacology | pharmacogenomics | pharmacology of natural products | signal transduction

The institute is located at Science Park I of Ulm University. Our Institute has 17 employees: 67% are female and 12.5% come from abroad. Six graduate students are currently attending our PhD program. We teach clinical and basic pharmacology to medical and basic sciences students.
The institute maintains a strong research profile using state-of-the-art equipment designed for demanding research projects that are often conducted in collaboration with other research groups on the campus as well as from abroad.

Our research profile is somewhat unusual and, to some extent, is the result of a concept unique to Ulm that combines clinical pharmacology with pharmacology and chemistry of natural products. Accordingly, the institute is subdivided into several research groups: chemistry and pharmacology of natural products; biochemical and immunopharmacology combined with protein chemistry, chemistry, pharmacology and toxicology of nanomaterials; and pharmacogenomics.
With respect to pharmacology of natural products, we isolate and characterize natural compounds with the goal of identifying lead compounds for the therapeutic modulation of signal transduction mechanisms in inflammation and cancer. We possess considerable expertise in the molecular characterization of small molecule-protein interactions by means of surface plasmon resonance analysis. Highly sensitive analytical methods allow us to analyze pharmacokinetics in minute amounts of plasma, e.g. in the circulation of chicken embryos.
Molecular pharmacological and biochemical studies are aimed at the elucidation of proteolytic signal transduction mechanisms in cells engaged in chronic inflammatory processes, which are the most frequent reasons for patients seeking medical treatment.

Nanomaterials offer a great range of opportunities. More recent studies in our institute were aimed at the characterization of the nano-bio interface. The insight obtained from those experiments was used to develop novel nanomaterials with exceptional and precisely defined physicochemical properties. We are currently exploring their potential therapeutic application in cancer treatment, Moreover, special nanomaterials have been designed and synthesized that might allow remote modulation of cell functions by external physical forces.

The group working on immunopharmacological topics deals primarily with the complement system as an effector of the innate immune system. The goal is to develop new immunological applications, e.g. novel complement inhibitors by protein biochemical and biopharmaceutical approaches. Accordingly, the methodology includes engineering and production of recombinant proteins as well as the testing of promising immunomodulatory biopharmaceutical candidates in terms of protein-protein and protein-cell interactions by employing state-of-the-art technologies.

The central research topic of the Clinical Pharmacology group of the institute (Prof. Dr. Oliver Zolk) is the identification of (genetic) markers, which allow prediction of “responder” and “non-responder” to a given pharmacotherapy. Marked differences are frequently observed in the treatment effects between individual patients that may lead to treatment failure or undesirable side-effects. Unlike standard therapy (“one-size-fits-all”), personalized therapy aims at identifying clinically relevant subpopulations of patients for a targeted treatment. Genetic, molecular or cellular markers are the basis for the selection of patients suitable for a specific therapy. We apply pharmacogenetic tests and advise physicians to adapt the therapy to the individual variations in the genetic profile of the patients.



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Selected Publications:

- *Loos C, Syrovets T, Musyanovych A, Mailänder V, Landfester K, Simmet Th (2014) Amino-functionalized nanoparticles as inhibitors of mTOR and inducers of cell cycle arrest in leukemia cells. Biomaterials 35:1944–1953.*
- *Park H, Guariento M, Maciejewski M, Hauhart R, Tham WH, Cowman A, Schmidt CQ, Mertens H, Liszweski K, Hourcade D, Barlow P, Atkinson J (2014) Using mutagenesis and structural biology to map the binding site for the Plasmodium falciparum merozoite protein PfRh4 on the human immune adherence receptor. J Biol Chem 289:450-463.*
- *Schmidt CQ, Bai H, Lin Z, Risitano A, Barlow P, Ricklin D, Lambris J (2013) Rational engineering of a minimized immune inhibitor with unique triple-targeting properties. J Immunol 11:5712-21.*
- *Müller I, Schönberger T, Schneider M, Borst O, Ziegler M, Seizer P, Leder C, Müller K, Lang M, Appenzeller F, Lunov O, Büchele B, Fahrleitner M, Olbricht M, Langer H, Geisler T, Lang F, Chatterjee M, de Boer JF, Tietge UJ, Bernhagen J, Simmet Th, Gawaz M (2013) Gremlin-1 is an inhibitor of macrophage migration inhibitory factor and attenuates atherosclerotic plaque growth in ApoE-/- mice. J Biol Chem 288:31635-45.*
- *Strobel J, Mueller F, Zolk O, Endress B, Koenig J, Fromm M, Maas R (2013) Transport of asymmetric dimethylarginine (ADMA) by cationic amino acid transporter 2 (CAT2), organic cation transporter 2 (OCT2) and multidrug and toxin extrusion protein 1 (MATE1). Amino Acids 45:989-1002.*

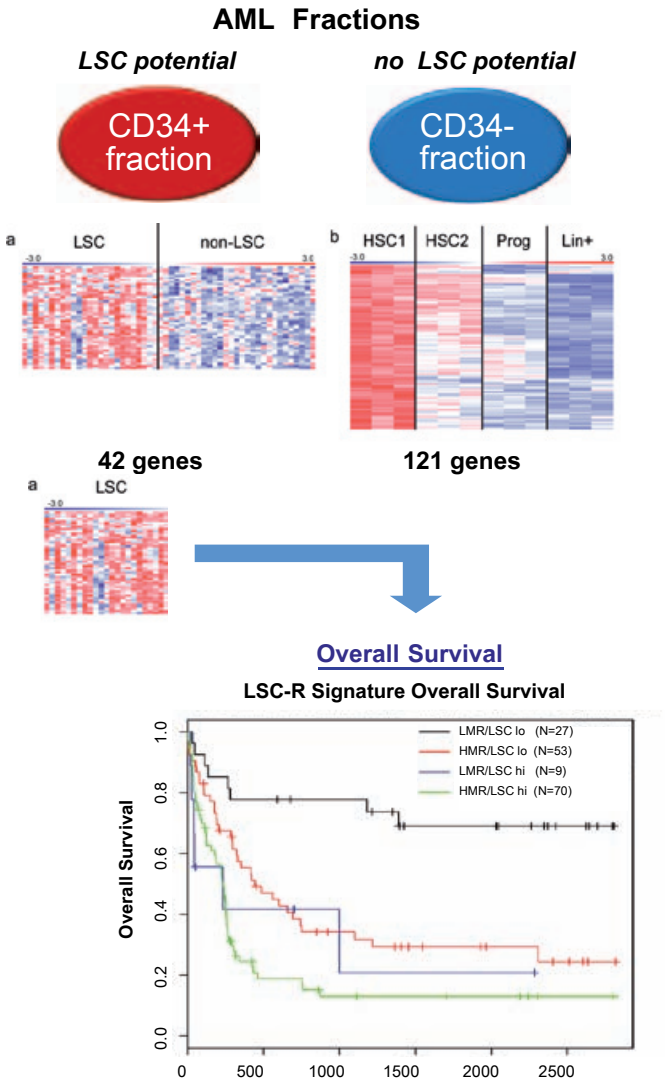

Figure 1: Gene expression signature of functionally validated leukemic stem cells isolated from patients with acute myeloid leukemia correlates with treatment outcome in patients with normal karyotype AML. LSC = leukemic stem cell

Institute of Experimental Cancer Research

Head of Institute: Prof. Dr. Christian Buske

Keywords: Leukemia | stem cell biology | lymphoma | WM | MZL

As a clinical institute of the Comprehensive Cancer Center Ulm (CCCU), our central goal is to advance translational research in tumor biology and to act as a bridge between research institutes of the university and the clinical departments of the university hospital. The focus of our research lies in the mechanisms of tumorigenesis by using acute leukemias as a model disease of cancer.
Another focus of the institute is clinical lymphoma research. The institute coordinates the newly founded "European Consortium for Waldenström's macroglobulinemia" (ECWM) and the national registry for marginal zone lymphoma in Germany that is funded by *Deutsche Krebshilfe* (German Cancer Aid).

Translational Research

Functional Analysis of Genetic Alterations in Acute Leukemia

We try to understand the mechanisms through which leukemia-specific genetic aberrations convert normal hematopoietic cells to leukemic cells by using appropriate mouse models mimicking human AML. The institute is particularly interested in leukemias induced by the AML1-ETO fusion gene, the NPM1 mutation or leukemogenic HOX genes, which are all aberrations found in patients with acute myeloid leukemia.

Importance of Non-coding RNA for Normal and Malignant Hematopoiesis

A further focus of our institute is to dissect the function of non-coding RNA molecules (RNA that do not encode proteins) in normal and malignant hematopoiesis. Using different in vivo models, our group aims to identify crucial differences in the expression of non-coding RNAs between healthy and leukemic stem cells and to clarify which microRNA acts as an oncogene and which one acts as a tumor suppressor gene.

Identification of Tumor Stem Cells

Another major focus of the institute lies in the characterization of leukemic stem cells and to define differences between healthy and leukemic stem cells. This would allow the development of therapeutic approaches which selectively kill leukemic stem cells.



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Characterization of Stem Cell Regulating Factors
The understanding of normal blood hematopoiesis is the basis for our understanding of malignantly transformed hematopoiesis. Hence, several projects deal with the question of determining which factors are crucial for the function of normal blood stem cells (Figure 1).

Clinical Research

Waldenström's Macroglobulinemia (WM)
The institute coordinates the "European Consortium for Waldenström's Macroglobulinemia" (ECWM) (www.ecwm.eu/), a European consortium in which all major study groups in Europe participate. The consortium initiated a large academic phase III trial to test the efficacy of Bortezomib in the first line of treatment of patients with WM (PI: Prof. C. Buske; sponsored by Ulm University Hospital).

Marginal Zone Lymphoma (MZL)
In 2014 the institute will open a national registry for marginal zone lymphoma. This registry aims at collecting data about the treatment and therapy outcome of patients suffering from MZL in Germany and is funded by *Deutsche Krebshilfe* (German Cancer Aid).

Early Trials Network (ETN)
The head of the institute is the speaker of the ETN, which is a network of university hospitals in Germany, supporting the initiation of early clinical trials in B-cell lymphomas (www.unimedizin-mainz.de/early-trials-network/overview.html).

Selected Publications:
- *Expression of the lymphoid enhancer factor 1 is required for normal hematopoietic stem and progenitor cell function. Edmaier KE, Stahnke K, Vegi N, Mulaw M, Ihme S, Scheffold A, Rudolph KL, Buske C. Leukemia. 2014;28(1):227-30.*
- *Buske C, Leblond V. How to manage Waldenström's macroglobulinemia. Leukemia. 2013;27(4):762-72.*
- *Metzeler KH, Heilmeier B, Edmaier KE, Rawat VPS, Dufour A, Doehner K, Feuring-Buske M, Braess J, Spiekermann K, Buchener T, Sauerland MC, Doehner H, Hiddemann W, Bohlander SK, Schlenk RF, Bullinger L, Buske C. High expression of lymphoid enhancer-binding factor-1 (LEF1) is a novel favorable prognostic factor in cytogenetically normal acute myeloid leukemia. Blood 2012; 120 (10): 2118 - 2126.*
- *Rawat VP, Humphries RK, Buske C. Beyond HOX: the role of ParaHOX genes in normal and malignant hematopoiesis. Blood. 2012 120(3): 519-527.*
- *Eppert K, Takenaka K, Lechman ER, Waldron L, Nilsson B, van Galen P, Metzeler KH, Poeppl A, Ling V, Beyene J, Canty AJ, Danska JS, Bohlander SK, Buske C, Minden MD, Golub TR, Jurisica I, Ebert BL, Dick JE. Stem cell gene expression programs influence clinical outcome in human leukemia. Nature Medicine 2011; 17: 1086-1093.*



Experimental setup for the virtual reality study at the Institute of Research in Rehabilitation Medicine at Ulm University, Bad Buchau.

Institute of Research in Rehabilitation Medicine at Ulm University

Head of Institute: Prof. Dr. Gert Krischak, MBA

Keywords: rehabilitation | health service evaluation | clinical research | administrative data | physical therapy

The Research Association for Rehabilitation Science Ulm focuses on the different phases of rehabilitation in Germany and the interdisciplinary points of intersection. The Institute of Research in Rehabilitation Medicine at Ulm University is a member of this research association and is located in Bad Buchau. It has 11 members who receive most of their funding from third parties. Research activities focus on several aspects of rehabilitation and prevention. Our core task is practice-oriented research and the transmission of the results to health care institutions.

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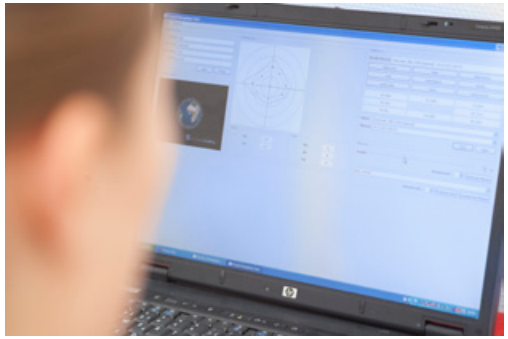
Our institute has three main fields of research:

Firstly, the health service research of Dr. biol.-hum. R. Kaluscha and the health service evaluation of S. Jankowiak, M.Sc. Public Health, analyze health processes and pilot projects in rehabilitation for effectiveness and feasibility. Moreover, they evaluate the results of medical and occupational rehabilitation to determine treatments. These can be used to make the rehabilitation more demand-actuated. The emphasis of many projects is the analysis of the administrative date of health and pension insurance.

Secondly, the clinical research of Dipl. Physioth. L. Tepohl, M.A., serves to create and evaluate different rehabilitation concepts. Furthermore, a clinical study within the development of a self-adapting treatment for continuous passive motion has just been initiated.

A third project of this team is a virtual reality study on the ability to train the fine motor movement control of the cervical spine for patients with chronic neck pain.



Selected Publications:

- *Neuner R, Braig S, Weyermann M, Kaluscha R, Krischak G (2013): Short-term goal attainment of in-patient rehabilitation in Germany and long-term risk of early retirement in patients with musculoskeletal diseases: results from a prospective 5-year follow-up study. Disabil Rehabil., 35(8): 656-61.*
- *Kraus M, Krischak G, Tepohl L. Postoperative rehabilitation of patients with shoulder arthroplasty- a review on the standard care. Int J Phys Med Rehabil 2014, Special Issue: Surgical Rehabilitation: 5: 001*
- *Krischak G, Gebhard F, Reichel H, Friemert B, Schneider F, Fisser C, Kaluscha R, Kraus M (2013): A prospective randomized controlled trial comparing occupational therapy with home-based exercises in conservative treatment of rotator cuff tears. J Shoulder Elbow Surg., 22(9): 1173-9.*
- *Krischak G, Kaluscha R, Kraus M, Tepohl L, Nusser M (2013): Return to work after total hip arthroplasty. Unfallchirurg, 116(8): 755-9.*
- *Neuner R, Braig S, Weyermann M, Kaluscha R, Krischak G (2012): Is Physicians Judgment on Short-Term Therapy Success Suitable to Predict Long-Term Working Capacity? Physikalische Medizin, Rehabilitationsmedizin, Kurortmedizin, 22(3): 147-153.*



Endoscopy

Department of Internal Medicine I

Head of Department: Prof. Dr. Thomas Seufferlein

Keywords: Gastroenterology | gastrointestinal oncology | hepatology | pancreatic diseases | endoscopy | nephrology | endocrine diseases

Our department specializes in the diagnosis and treatment of patients with diseases of the GI tract such as gastrointestinal tumors (including neuroendocrine tumors of the GI tract), diseases of the liver, inflammatory bowel disease, endocrine disorders and diabetes, as well as acute and chronic kidney diseases. A special focus is centered on all diagnostic and therapeutic endoscopic procedures and transcutaneous as well as endoscopic ultrasound.

The department has 160 employees comprising 50 MDs and scientists, and 110 nurses and technical staff. We take care of four wards in Internal Medicine with 98 beds and are responsible for the Emergency Room of the Center for Internal Medicine. The department runs specialized outpatient clinics for GI oncology, IBD, hepatology, endoscopy, endocrine diseases, diabetes and nephrology including renal transplantation. More than 4,400 inpatients and 14,000 outpatients are treated in the department each year.

Our scientific focus in basic science is on gastrointestinal carcinogenesis and tumor promotion, particularly in pancreatic and liver cancer. We investigate the basic mechanisms of metastasis and protein transport, stem cell biology, and the immunological basis of type I diabetes. In translational and clinical research we run biomarker programs in several entities and aim at establishing novel means to monitor drug-induced tumor evolution in patients. Clinical trials are run in all clinical areas of the department (GI oncology, IBD, hepatology, endocrinology, nephrology). More than 50 national

and international phase I-IV trials are currently active in our Clinical Trials Unit. Several are being led by investigators of our department.

We receive national and international grants and participate in numerous national and international research collaborations. In the field of GI oncology the department is part of the Comprehensive Cancer Center Ulm (CCCU) and all patients are assessed by a multidisciplinary team. The Interdisciplinary Bowel Cancer Center, which is led by the department, was the second of these centers certified by the German Cancer Society. We closely cooperate with colleagues from surrounding community hospitals and general practices.

Our therapeutic standards follow national and international guidelines and the department actively contributes to the formulation of many of these guidelines.



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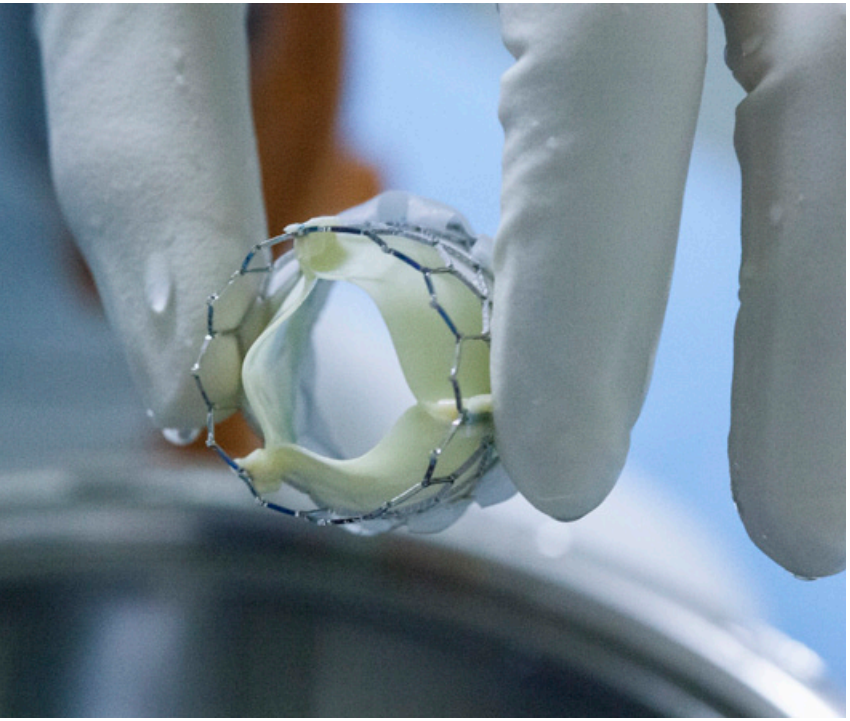
Selected Publications:

- *[S3-guideline exocrine pancreatic cancer]. Seufferlein T, Porzner M, Becker T, Budach V, Ceyhan G, Esposito I, Fietkau R, Follmann M, Friess H, Galle P, Geißler M, Glanemann M, Gress T, Heinemann V, Hohenberger W, Hopt U, Izbicki J, Klar E, Kleeff J, Kopp I, Kullmann F, Langer T, Langrehr J, Lerch M, Löhr M, Lüttges J, Lutz M, Mayerle J, Michl P, Möller P, Molls M, Münter M, Nothacker M, Oettle H, Post S, Reinacher-Schick A, Röcken C, Roeb E, Saeger H, Schmid R, Schmiegel W, Schoenberg M, Siveke J, Stuschke M, Tannapfel A, Uhl W, Unverzagt S, van Oorschot B, Vashist Y, Werner J, Yekebas E. Z Gastroenterol. 2013 Dec;51(12):1395-440.*
- *Protein Kinase D2 induces invasion of pancreatic cancer cells by regulating matrix metallo-proteinases.Wille C, Köhler C, Armacki M, Jamali A, Gössele U, Pfizenmaier K, Seufferlein T, Eiseler T. Mol Biol Cell. 2013 Dec 11.*
- *A novel splice variant of calcium and integrin-binding protein 1 mediates protein kinase D2-stimulated tumour growth by regulating angiogenesis. Armacki M, Joodi G, Nimmagadda SC, de Kimpe L, Pusapati GV, Vandoninck S, Van Lint J, Illing A, Seufferlein T. Oncogene. 2013 Mar 18.*
- *A missing PD-L1/PD-1 coinhibition regulates diabetes induction by preproinsulin-specific CD8 T-cells in an epitope-specific manner. Schuster C, Brosi H, Stifter K, Boehm BO, Schirmbeck R. PLoS One. 2013 Aug 19;8(8):e71746.*
- *Increased reprogramming capacity of mouse liver progenitor cells, compared with differentiated liver cells, requires the BAF complex. Kleger A, Mahaddalkar PU, Katz SF, Lechel A, Joo JY, Loya K, Lin Q, Hartmann D, Liebau S, Kraus JM, Cantz T, Kestler HA, Zaehres H, Schöler H, Rudolph KL. Gastroenterology. 2012 Apr;142(4):907-17.*

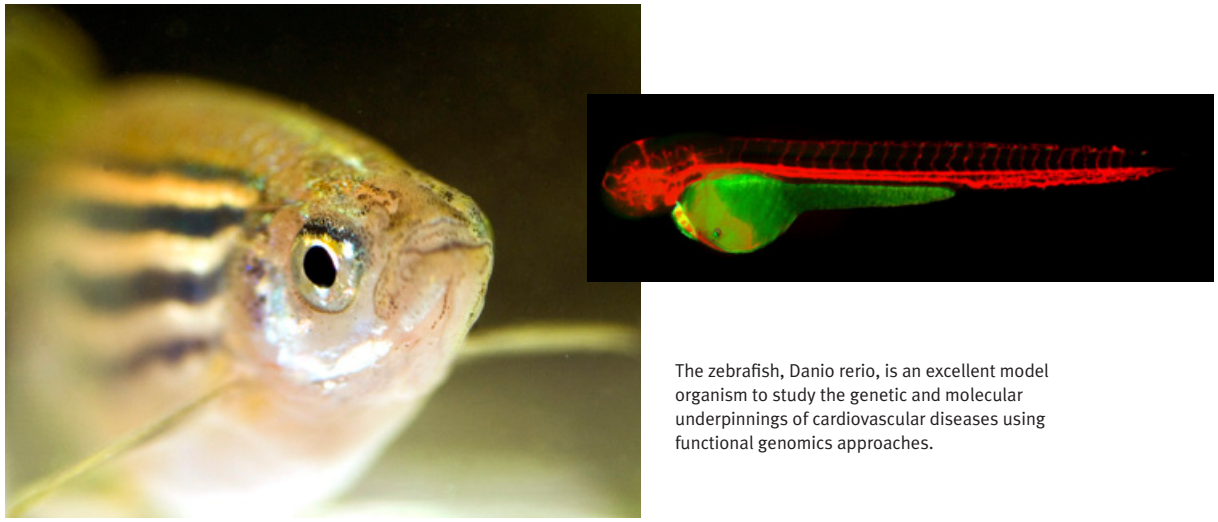


Department of Internal Medicine II

Head of Department: Prof. Dr. Wolfgang Rottbauer
Keywords: Basic vascular and myocardial research | innovative cardiovascular imaging | interventional cardiovascular medicine

The department comprises the divisions of Cardiology, Angiology, Intensive Care Medicine, and two subdivisions: Pneumology (Head: PD Dr. Schumann, since April 1, 2014, Dr. Kropf-Sanchen) and Sports and Rehabilitation Medicine (Head: Prof. Dr. Steinacker). It represents these areas in inpatient and outpatient care, clinical and basic research, and in teaching and medical education (86 regular ward beds, five beds for monitoring sleep disorders, 52 telemetry options and 12 ICU beds). There are currently 49 full-time physicians, two physicists, 29 technical assistants and data managers who mainly work in the clinical routine. In addition, there are 11 technical assistants and six study nurses, both part-time and full-time, employed in clinical and basic research. Currently, there are 15 PhD students trained in the different scientific research groups.

The Cardiology and Angiology Division offers the whole spectrum of modern non-invasive and invasive diagnostic and interventional procedures. In the four cath labs, besides routine and emergency percutaneous interventions on coronary and peripheral arteries, including renal and carotid arteries, complex interventional procedures, such as revascularization of chronic total occlusions, percutaneous aortic valve replacement and mitral repair as well as occlusion of patent foramen ovale or atrial/ventricular septal defects, are routinely provided. The electrophysiology group implants approximately 300 pacemakers and ICDs annually and in addition appr. 80 CRTs. In the electrophysiology suite, about 300 radiofrequency ablations of supraventricular and ventricular tachycardias are annually performed. The department houses two cardiac MRI scanners (1.5 Tesla and 3.0 Tesla) and performs about 2,000 cardiovascular scans annually. In the Pneumology Subdivision, all modern diagnostic and interventional techniques as well as innovative therapeutic strategies have been implemented for the treatment of lung diseases, especially lung cancer. The Sports and Rehabilitation Medicine Subdivision offers outpatient clinics for a variety of sports disciplines and supervises many athletes and national teams. In addition, it offers ambulatory cardiac rehabilitation, in particular, post-myocardial infarction and post-cardiovascular surgery.



The zebrafish, Danio rerio, is an excellent model organism to study the genetic and molecular underpinnings of cardiovascular diseases using functional genomics approaches.

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The department runs the core facility for small animal imaging of the Medical Faculty. Here, cutting edge MRI and µCT imaging and spectroscopy capabilities are provided for non-invasive assessment of disease stages in small animals

Biomedical research is embedded in national and international research networks and consortia, and focuses on vascular pathologies and diseases of the heart muscle, including cardiomyopathies and arrhythmias, and, in particular, on the related genetic etiology and molecular pathophysiology. Large scale population-based genome-wide association studies as well as genomics and metabolomics of myocardial infarction and, in particular, of inflammatory processes are also covered. State-of-the-art functional genomics approaches in animal models, such as mice and zebrafish, have been established to study particularly the molecular basis of heart development and regeneration. Furthermore, animal models, such as LDL-receptor knock-out mice, apoE deficient mice as well as murine acute myocardial infarction models, are well established in the research department.

Clinical research is coordinated by a clinical trial unit that allows recruitment and monitoring of large patient cohorts in innovative trials with novel cardiometabolic compounds according to FDA or EMEA standards. Our preventive cardiology program focuses on the identification and evaluation of new biomarkers for cardiometabolic diseases. The experimental cardiovascular imaging group, comprising MR scientists and clinical MR experts, concentrates on the assessment of the role of MRI for the diagnosis of cardiovascular diseases. Techniques for tissue characterization and new approaches for the early identification and quantification of the significance of myocardial ischemia and myocardial motion abnormalities have been developed and are evaluated for their clinical utility.

Selected Publications:

- *Nicholls SJ, Kastelein JJ, Schwartz GG, Bash D, Rosenson RS, Cavender MA, Brennan DM, Koenig W, Jukema JW, Nambi V, Wright RS, Menon V, Lincoff AM, Nissen SE; for the VISTA-16 Investigators. Varespladib and Cardiovascular Events in Patients With an Acute Coronary Syndrome: The VISTA-16 Randomized Clinical Trial. JAMA. 2013 Nov 18. doi: 10.1001/jama.2013.282836. [Epub ahead of print]*
- *Thiele H, Wöhrle J, Hambrecht R, Rittger H, Birkemeyer R, Lauer B, Neuhaus P, Brosteanu O, Sick P, Wiemer M, Kerber S, Kleinertz K, Eitel I, Desch S, Schuler G. Intracoronary versus intravenous bolus abciximab during primary percutaneous coronary intervention in patients with acute ST-elevation myocardial infarction: a randomised trial. Lancet. 2012;379:923-31.*
- *Lutz A, Paul J, Bornstedt B, Nienhaus GU, Etyngier P, Bernhardt P, Rottbauer W, Rasche V. Volumetric motion quantification by 3D tissue phase mapped MRI. J Cardiovasc Magn Reson. 2012; 4:74.*
- *Keller A, Leidinger P, Bauer A, Elsharawy A, Haas J, Backes C, Wendschlag A, Giese N, Tjaden C, Ott K, Werner J, Hackert T, Ruprecht K, Huwer H, Huebers J, Jacobs G, Rosenstiel P, Dommisch H, Schaefer A, Müller-Quernheim J, Wullich B, Keck B, Graf N, Reichrath J, Vogel B, Nebel A, Jager SU, Staehler P, Amarantos I, Boisguerin V, Staehler C, Beier M, Scheffler M, Büchler MW, Wischhusen J, Haeusler SF, Dietl J, Hofmann S, Lenhof HP, Schreiber S, Katus HA, Rottbauer W, Meder B, Hoheisel JD, Franke A, Meese E. Toward the blood-borne miRNome of human diseases. Nat Methods. 2011;8:841-3.*
- *Just S, Berger IM, Meder B, Backs J, Keller A, Marquart S, Frese K, Patzel E, Rauch GJ; Tübingen 2000 Screen Consortium, Katus HA, Rottbauer W. Protein kinase D2 controls cardiac valve formation in zebrafish by regulating histone deacetylase 5 activity. Circulation. 2011;124:324-34.*



Department of Internal Medicine III

Head of Department: Prof. Dr. Hartmut Döhner

Keywords: Biology | leukemial lymphoma | therapy | tumor

The Department of Internal Medicine III has its focus on the diagnosis and treatment of diseases in the fields of hematology, oncology, palliative care, rheumatology and infectious diseases. The department is one of the largest of its kind in Germany with 110 inpatient beds, outpatient facilities and over 250 employees involved in patient care, research, teaching and education.

Specialized clinical care is provided for patients with benign and malignant disorders of the hemato-lymphopoietic system (e.g. anemia, acute and chronic leukemias, myelodysplastic syndromes, myeloproliferative diseases, Hodgkin-/non-Hodgkin lymphomas, multiple myeloma, aplastic anemia) and of patients with various solid tumors (e.g. lung cancer, renal cell carcinoma, breast cancer, brain tumors, sarcomas, germ cell tumors). Solid tumor activities are coordinated in a dedicated Oncology Section. The spectrum of activities comprises all modern diagnostic and therapeutic approaches, such as conventional chemotherapies, innovative treatments with monoclonal antibodies, biologicals, molecular-targeted approaches with novel compounds, and bone marrow/peripheral blood stem cell transplantation. The transplant unit is among the most experienced in the world. Another focus of the department is on the treatment of patients with hemophilia and thrombophilia, and of patients with autoimmune/rheumatologic diseases. The Section of Infectious Diseases is focused on the treatment of a wide range of patients, in particular HIV/AIDS, tuberculosis, tropical diseases, and echinococcosis. It provides vaccination and consultation services for travelers to foreign countries. It is both a partner and leader of the Comprehensive Infectious Disease Centre (CIDC).

Research activities include basic scientific as well as translational aspects with a focus on the identification and characterization of molecular pathogenesis, and on the development of novel therapies. A wide spectrum of clinical trials is active and thus continuously offers access to

innovative treatments in hematology and oncology to ensure the highest quality of patient care. Medical doctors and scientists from our department are nationally and internationally renowned for their research work. This was documented in 2013 by the publication of over 200 articles in various international scientific journals, the obtaining of more than seven million euros in external research grant funding, and by participation in the development of international guidelines.
A major structure to advance laboratory science is the SFB1074 (coordinating principal investigator: H. Döhner) entitled "Experimental models and clinical translation in leukemia" (see separate article and http://www.uni-ulm.de/en/einrichtungen/sfb-1074.html).

The Laboratory for Cytogenetic and Molecular Genetic Diagnostics is a central reference laboratory within a number of multicenter clinical trial groups, e.g. the German-Austrian AML Study Group (AMLSG), the German Myeloproliferative Neoplasms Group (MPNSG), the German CLL Study Group (GCLLSG) and the German Multiple Myeloma Study Group (DSMM), as well as within various international pharmaceutical industry-sponsored trials.

To promote clinical research, the department hosts a Clinical Trials Unit (CTU) with a team of highly trained medical doctors and oncology study nurses. About 100 clinical trials of phase I-II (early development of novel and promising anti-cancer agents) and of phase III (randomized treatment trials) are currently active. A large proportion of patients are treated within clinical trials to promote innovation and ensure the highest quality of patient care. The department is an active partner of the Comprehensive Cancer Center Ulm (CCCU).



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Selected Publications:

- *Lo-Coco F, Avvisati G, Vignetti M, Thiede C, Orlando SM, Iacobelli S, Ferrara F, Fazi P, Cicconi L, Di Bona E, Specchia G, Sica S, Divona M, Levis A, Fiedler W, Cerqui E, Breccia M, Fioritoni G, Salih HR, Cazzola M, Melillo L, Carella AM, Brandts CH, Morra E, von Lilienfeld-Toal M, Hertenstein B, Wattad M, Lübbert M, Hänel M, Schmitz N, Link H, Kropp MG, Rambaldi A, La Nasa G, Luppi M, Ciceri F, Finizio O, Venditti A, Fabbiano F, Döhner K, Sauer M, Ganser A, Amadori S, Mandelli F, Döhner H, Ehninger G, Schlenk RF,* Platzbecker U;* Gruppo Italiano Malattie Ematologiche dell' Adulto, the German–Austrian Acute Myeloid Leukemia Study Group, and Study Alliance Leukemia. Retinoic Acid and Arsenic Trioxide for Acute Promyelocytic Leukemia. N Engl J Med. 2013 Jul 11;369(2):111-121. (* equal contribution)*
- *Schnaiter A, Paschka P, Rossi M, Zenz T, Bühler A, Winkler D, Cazzola M, Döhner K, Edelmann J, Mertens D, Kless S, Mack S, Busch R, Hallek M, Döhner H, Stilgenbauer S. NOTCH1, SF3B1 and TP53 mutations in fludarabine-refractory CLL patients treated with alemtuzumab: results from the CLL2H trial of the GCLLSG. Blood. 2013 Aug 15;122(7):1266-70.*
- *Krönke J, Bullinger L, Teleanu V, Tschürtz F, Gaidzik VI, Kühn MW, Rücker FG, Holzmann K, Paschka P, Kapp-Schwörer S, Späth D, Kindler T, Schittenhelm M, Krauter J, Ganser A, Göhring G, Schlegelberger B, Schlenk RF, Döhner H, Döhner K. Clonal evolution in relapsed NPM1 mutated acute myeloid leukemia. Blood. 2013 Jul 4;122(1):100-8.*
- *Faber K, Bullinger L, Ragu C, Garding A, Mertens D, Miller C, Martin D, Walcher D, Döhner K, Döhner H, Claus R, Plass C, Sykes SM, Lane SW, Scholl C, Fröhling S. CDX2-driven leukemogenesis involves KLF4 repression and deregulated PPAR? signaling. J Clin Invest. 2013 Jan 2;123(1):299-314.*
- *Gröschel S, Schlenk RF, Engelmann J, Rockova V, Teleanu V, Kühn WM, Eiwen K, Erpelinck C, Havermans M, Lübbert M, Germing U, Schmidt-Wolf IGH, Berna Beverloo H, Schuurhuis GJ, Ossenkoppele GJ, Schlegelberger B, Krauter J, Ganser A, Valk PJM, Löwenberg B, Döhner K, Döhner H*, Delwel R*, Deregulated expression of EVI1 defines a poor prognostic subset of MLL-rearranged acute myeloid leukemias: a study of the German-Austrian AMLSG and Dutch-Belgian HOVON groups. J Clin Oncol. 2013 Jan 1;31(1):95-103. (* equal contribution)*



Institute of Transfusion Medicine

Head of Institute: Prof. Dr. Hubert Schrezenmeier

Keywords: Hemapoietic stem cells | mesenchymal stromal cells | molecular diagnostics | transfusion

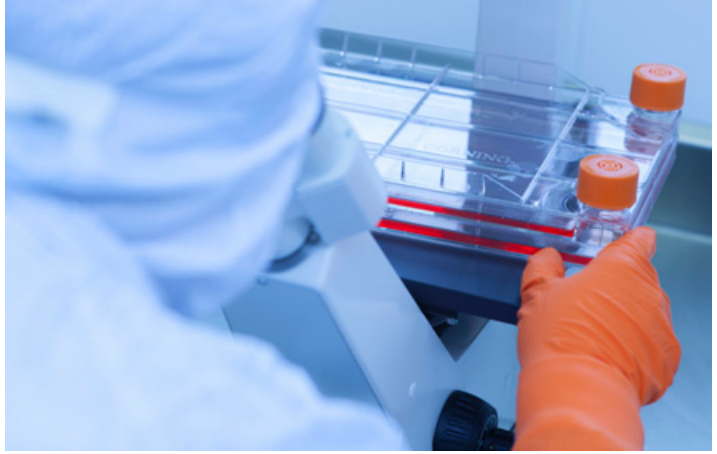
The institute is supported by the German Red Cross Blood Transfusion Service Baden-Wuerttemberg-Hessia and acts in close collaboration with the Institute of Clinical Transfusion Medicine and Immunogenetics Ulm (IKT Ulm) as a joint venture of the German Red Cross Blood Donor Transfusion Baden-Wuerttemberg-Hessia and the University Hospital of Ulm.

Research activities focus on two fields:

- Molecular diagnostics in immunogenetics, blood group genotyping, and defects of hematopoiesis and the immune system,
- Advanced therapy medicinal products (ATMP): development of large-scale GMP grade selection, manipulation, and cell expansion for regenerative therapy and immunotherapy.

In the work group “Molecular Pathophysiology, Molecular Diagnostics and Experimental Transplantation” new disease-causing mutations and pathophysiology of severe inborn errors of the immune system and hematopoiesis have been deciphered. Methods are developed for gene repair with oligodeoxynucleotides in these disorders. Also pathophysiology of hemolytic disorders and acquired bone marrow failure syndromes is studied with the aim to improve outcome by treatments targeting the complement system or modulating the immune system.

The Department of Transplantation Immunology focuses on optimized donor-recipient matching in order to improve outcome after stem cell transplantation. Therefore, methods for sequenced-based typing of HLA-A, -B, -C and HLA-DRB1 and –DQB1, a CE-certified kit for efficient high throughput HLA-typing as well as methods for typing also non-classical HLA molecules and non-HLA gene polymorphisms have been developed. The impact of single and combined HLA allele mismatches, Null-alleles and non-classical HLA alleles or non-HLA-gene polymorphisms on outcome after allogeneic stem cell transplantation is analysed.



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In the Department of Blood Group Serology and Immunohematology, the genetic basis of the RhD-negative and weak-D phenotype and many new variants in the Rhesus blood group system has been elucidated. Methods for blood group genotyping have been developed.

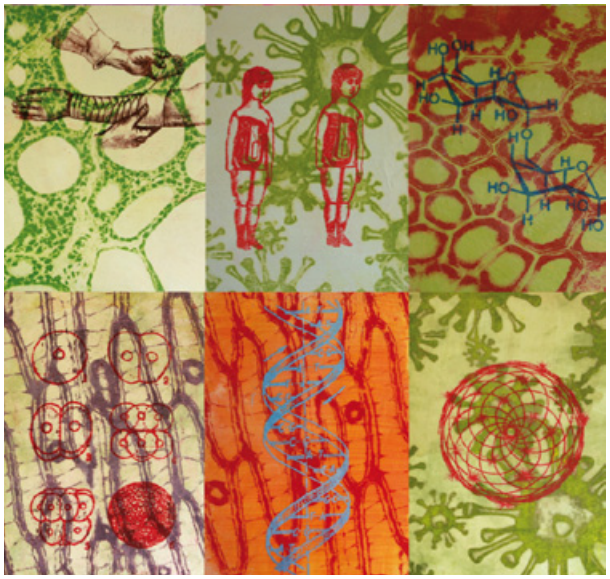
Activities in the Department of Stem Cells and Cellular Therapy include the collection of peripheral blood stem cells, selection of CD34-positive hematopoietic progenitor cells, lymphocyte depletion of stem cell preparations as well as preparations for adoptive immunotherapy (donor lymphocytes, opsonized lymphocytes, dendritic cells). A main area of research is the functional characterization and ex vivo expansion of mesenchymal stroma cells (MSC) for regenerative and immunomodulatory therapy. Different large-scale GMP-grade, xenogen-free protocols for efficient ex vivo expansion of MSC up to > 1 x 10^8 cells have been developed. Regulatory approval for use of these ATMPs has been obtained. Our GMP clean room is one production site within a European Network funded by the seventh Framework Program of the European Commission. In the REBORNE project, MSC are explored in clinical trials for their potential in bone healing in close cooperation with the Department of Trauma Surgery Research and Biomechanics, the Department of Orthopedic Trauma, Hand, Plastic and Reconstructive Surgery, and the Department of Internal Medicine II.

We also explore how MSC, non-classical granzyme B-expressing cells and regulatory B-cells modulate the immune system and might be used for immunotherapy.

The IKT Ulm delivers the whole range of blood products and stem cell preparations and the diagnostics in the field of transfusion and transplantation medicine (blood group typing, immunohematology, transplantation immunology) for the University Hospital of Ulm and many other medical facilities in Baden-Wuerttemberg.

Selected Publications:

- *Pannicke U, Baumann B, Fuchs S, Henneke P, Rensing-Ehl A, Rizzi M, Janda A, Hese K, Schlesier M, Holzmann K, Borte S, Laux C, Rump E-M, Rosenberg A, Zelinski T, Schrezenmeier H, Wirth T, Ehl S, Schroeder ML, Schwarz K (2013): Deficiency of innate and acquired immunity caused by an IKBKB mutation. New Engl J Med, 369: 2504-2514.*
- *Fürst D, Müller C, Vucinic V, Bunjes D, Herr W, Gramatzki M, Schwerdtfeger R, Arnold R, Einsele H, Wulf G, Pfreundschuh M, Glass B, Schrezenmeier H, Schwarz K, Mytilineos J (2013): High resolution HLA-matching in hematopoietic stem cell transplantation: a retrospective collaborative analysis. Blood, 122: 3220-3229.*
- *Krawitz PM, Höchsmann B, Murakami Y, Teubner B, Krüger U, Klopocki E, Neitzel H, Hoellein A, Schneider C, Parkhomchuk D, Hecht J, Robinson PN, Mundlos S, Kinoshita T, Schrezenmeier H (2013): A case of paroxysmal nocturnal hemoglobinuria caused by a germline mutation and a somatic mutation in PIGT. Blood, 122: 1312-1315.*
- *Lindner S, Dahlke K, Sontheimer K, Hagn M, Kaltenmeier C, Barth TF, Beyer T, Reister F, Fabricius D, Lotfi R, Lunov O, Nienhaus GU, Simmet T, Kreienberg R, Möller P, Schrezenmeier H, Jahrsdörfer B (2013): Interleukin 21-induced granzyme B-expressing B cells infiltrate tumors and regulate T cells. Cancer Res, 73: 2468-2479.*
- *Fekete N, Rojewski MT, Fürst D, Kreja L, Ignatius A, Dausend J, Schrezenmeier H (2013): GMP-compliant isolation and large-scale expansion of bone marrow-derived MSC. PLoS One 7: e43255.*



Artwork by Stefanie Siering

Illustration for the XX Annual Meeting of the German Society for Gene Therapy (DG-GT).

Department of Gene Therapy

Head of Department: Prof. Dr. Stefan Kochanek

Keywords: Somatic gene therapy | genetic vaccination | vector production | neurodegenerative diseases

The mission of the Department of Gene Therapy is to conduct high quality research and teaching in different research aspects of somatic gene therapy, genetic vaccination, development of gene transfer technologies and neurodegenerative diseases.
The development of novel vector technologies is the focus of current research activities and several projects in the laboratory aim at increasing efficiency, specificity and safety of therapeutic gene transfer.
Since viruses have evolved together with their hosts, they are by nature very efficient vehicles for the delivery of nucleic acids into cells. By removing one or several essential viral genes, they are converted to gene transfer vectors with improved safety. Using adenovirus as a well-characterized model virus, several projects relate either to the improvement of adenovirus vectors or to their use in different genetic and non-genetic diseases.

Overcoming gene therapy barriers

So far, in vivo gene therapy has been successful only in a small number of clinical studies and one of the main reasons for this is the lack of efficient gene transfer in vivo due to the interaction of vector particles with different barriers in blood and tissues. This problem is being addressed by several projects.

For example, genetic and chemical modification of adenovirus vectors, alone or in combination, is used to identify and to overcome barriers imposed by either cellular components in blood or tissues (erythrocytes, platelets, macrophages) or non-cellular components (antibodies and plasma proteins) which prevent efficient gene delivery to specific cell types.

Another focus of the laboratory is the development of oncolytic viruses for the treatment of solid cancers and the testing of these vectors in improved models of pancreatic cancer. Oncolytic viruses multiply within tumor cells and spread from cell to cell while destroying the tumor cells. These studies take into account the complex composition of solid tumors that, in addition to neoplastic cells, contain many other cell types, such as stromal cells and endothelial cells, and also an extracellular matrix.

Genetic vaccination for very common infectious diseases

Genetic vaccination shows considerable potential as a solution to overcome the limitations of classical vaccines in diseases like AIDS, tuberculosis and malaria. However, neither the mechanisms of induction nor the persistence of adaptive immune responses are understood very well following genetic vaccination. Based on the observation that the immunogenicity of adenovirus vectors negatively influences T-cell responses raised against vaccine antigens, we perform experiments to better understand basic mechanisms of genetic vaccination with the ultimate goal of improving the immunogenicity of genetic vaccines.

Biotechnology: production of viral vectors

Several projects concern biotechnological topics.

One of our long-standing interests is the immortalization of primary human cells from amniotic fluid under well-defined conditions and documentation with the aim to generate cell lines for industrial production of viral and, in particular, adenoviral vectors in clinical quality.

In a different project we wish to develop an improved and scalable production system for vectors based on Adeno-Associated Virus (AAV). This vector type is currently used in many clinical studies for the treatment mainly of genetic diseases. However, current production systems are very cumbersome and improved systems for production at an industrial scale are urgently needed.

Basic research and model development in neurodegenerative diseases

Besides performing treatment-directed research, we also have a strong interest in studying basic aspects of the pathogenesis of two neurodegenerative disorders: Huntington's disease (HD) and Parkinson's disease (PD). For these diseases, there are either no (HD) or only symptomatic (PD) therapies available. In HD we try to better understand the function of the protein that, in the case of mutation in the corresponding gene, causes disease. In PD we are developing improved models mimicking the disease as a basis for the identification of drugs with improved activities.



Artwork by Stefanie Siering

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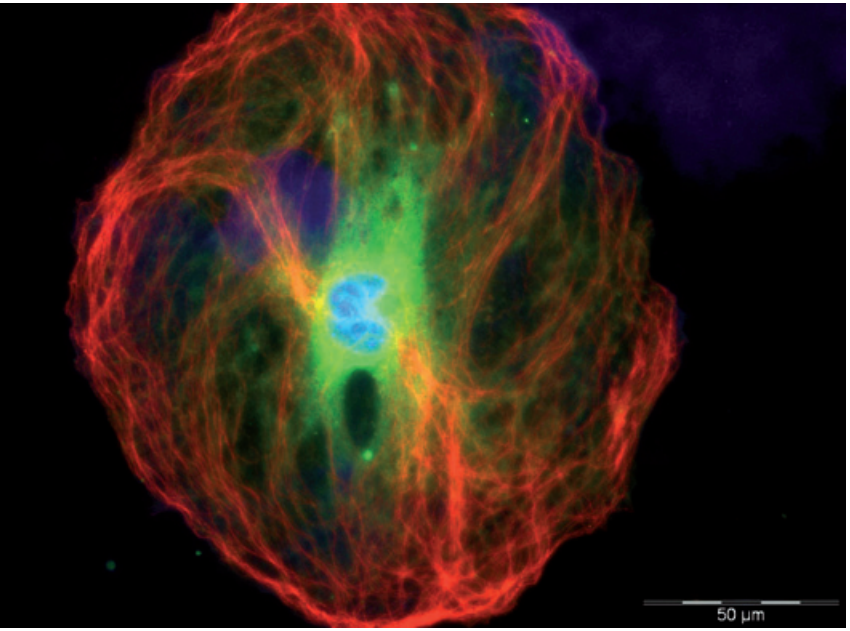
Selected Publications:

- *Prill JM, Subr V, Pasquarelli N, Engler T, Hoffmeister A, Kochanek S, Ulbrich K, Kreppel F. Traceless Bioresponsive Shielding of Adenovirus Hexon with HPMA Copolymers Maintains Transduction Capacity In Vitro and In Vivo. PLoS One. 2014 Jan 27;9(1):e82716.*
- *Laakkonen JP, Engler T, Romero IA, Weksler B, Couraud PO, Kreppel F, Kochanek S. Transcellular targeting of fiber- and hexon-modified adenovirus vectors across the brain microvascular endothelial cells in vitro. PLoS One. 2012;7(9):e45977.*
- *Dong X, Zong S, Witting A, Lindenberg KS, Kochanek S, Huang B. Adenovirus vector-based in vitro neuronal cell model for Huntington's disease with human disease-like differential aggregation and degeneration. J Gene Med. 2012 Jul;14(7):468-81.*
- *Zong S, Kron MW, Epp C, Engler T, Bujard H, Kochanek S, Kreppel F. ΔE1 and high-capacity adenoviral vectors expressing full-length codon-optimized merozoite surface protein 1 for vaccination against Plasmodium falciparum. J Gene Med. 2011 Dec;13(12):670-9*
- *Kron MW, Espenlaub S, Engler T, Schirmbeck R, Kochanek S, Kreppel F. miRNA-mediated silencing in hepatocytes can increase adaptive immune responses to adenovirus vector-delivered transgenic antigens. Mol Ther. 2011 Aug;19(8):1547-57.*



Effect of CK1 specific inhibitor 17 on the subcellular localization of CK1δ and CK1ε in MEFs. Primary mouse fibroblasts (MEFs) were either untreated or treated for 12 hours with a CK1 specific inhibitor (compound 17). To detect CK1δ (green) and α/β tubulin (red), fixed cells were incubated with specific primary antibodies and fluorescence-labeled secondary antibodies. DNA (blue) was stained with DAPI.

Department of General and Visceral Surgery

Head of Department: Prof. Dr. Doris Henne-Bruns

Keywords: Colorectal Cancer | Gastrointestinal Stroma Tumors | Gastric Cancer| Pancreatic Cancer | Surgical Oncology | Sepsis | Signal Transduction | Kinase inhibitors

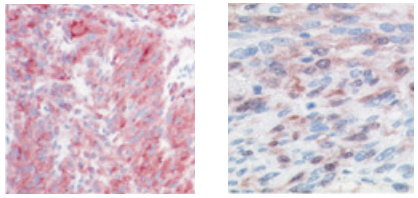
The Department of General and Visceral Surgery employs 33 physicians for 76 patient beds that are appointed on two regular wards, a special ward for children, and a surgical intensive care unit. Our focus is on surgical oncology and all standard procedures of general, visceral and endocrine surgery are performed. Special fields of expertise are hepato-biliary, pancreatic and colorectal surgery. The department also includes a section in pediatric surgery (Dr. med. C. Leriche).

The research interests of the individual research groups (M. Kornmann, MD, U. Knippschild, PhD, A. Formentini, MD, S. Paschke, MD, N. Huber, MD, J. Lemke, MD) are mainly focused on malignant diseases, and especially on pancreatic, gastric and colorectal carcinoma, and GIST, with foci on the characterization of alterations in signal transduction pathways, the characterization of biophysical properties of tumor cells, the identification of new target molecules for drug development, and the validation of kinase inhibitors *in vitro*, cell cultures, and animal models. Furthermore, additional projects concentrate on the analysis of the influence of changes in the expression of adipocytokines on septic progression (A. Hillenbrand, MD, A.-M. Wolf, MD and U. Knippschild, PhD), and the role of obesity as a disturbing factor during regeneration of muscle injuries (U. Knippschild in co-operation with M. Wabitsch, Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics and Adolescent Medicine, University of Ulm). Many of the projects are currently funded by the *Deutsche Forschungsgemeinschaft* (M. Kornmann, U. Knippschild), the *Deutsche Krebshilfe* (U. Knippschild), and the *Forschungsförderung des Landes Baden-Württemberg* (S. Paschke). In co-operation with the biotechnology company 4SC Discovery (Martinsried, Munich), several highly potent CK1 isoform specific inhibitors have been identified and characterized *in vitro*, in tissue culture and in animal

models. So far, these results have led to several publications in international journals. Since the identified inhibitors exhibit a high therapeutical potential, they can be integrated into new therapy concepts for the treatment of cancer and neurodegenerative diseases in the near future.

At present, two postdocs (J. Bischof, and Pengfei Xu) are working in the laboratories. Furthermore, students from EU countries, China, Costa Rica and Cameroon are completing either an experimental Bachelor, Master, PhD or MD thesis. A variety of cell culture, molecular biological and biochemical methods as well as several different animal models (xenotransplantation and transgenic models) for breast, colon and pancreatic cancer have been established. Furthermore, high-throughput techniques are used to identify molecules influencing the activity of protein kinases. Another special feature of the department is the availability of a large tissue bank that includes tumor, normal and fat tissues as well as the clinical data of patients.

In addition to this basic and translational research, our department currently participates in clinical multicenter trials concerning colon and rectal cancer.



Gastrointestinal stromal tumor (GIST)

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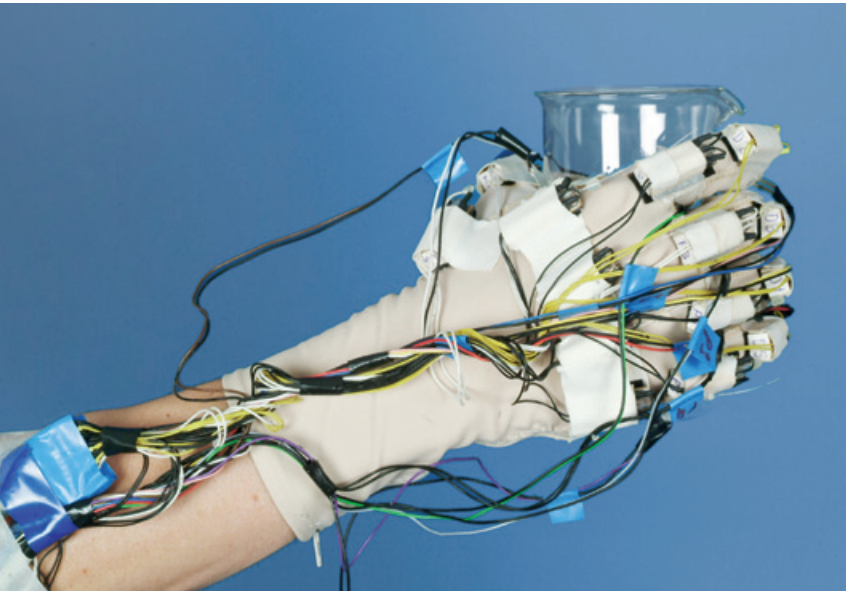
Selected Publications:

- *Lemke J, von Karstedt S, Abd El Hay M, Conti A, Arce F, Montinaro A, Papenfuss K, El-Bahrawy MA, Walczak H. Selective CDK9 inhibition overcomes TRAIL resistance by concomitant suppression of cFlip and Mcl-1. Cell Death Differ. 2014; 21:491-502. Epub 2013 Dec 20.*
- *Kornfeld J-W, Baitzel C, Könner A, Nicholls H, Vogt M, Herrmanns K, Scheja L, Haumaitre C, Wolf AM, Knippschild U, Seibler J, Cereghini S, Heeren J, Stoffel M, Brüning JC. Obesity-Induced Overexpression of miR-802 Impairs Glucose Metabolism Via Posttranscriptional Silencing of Tcf2/Hnf1β. Nature 2013; 494:111-5.*
- *Bischof J, Randoll SJ, Süßner N, Henne-Bruns D, Pinna LA, Knippschild U. CK1δ kinase activity is modulated by Chk1-mediated phosphorylation. PLoS One. 2013;8:e68803.*
- *Kornmann M, Hebart H, Danenberg K, Goeb R, Staib L, Kron M, Henne-Bruns D, Danenberg P, Link KH. Response prediction in metastasised colorectal cancer using intratumoural thymidylate synthase: results of a randomised multicentre trial. Eur J Cancer 2012; 48:1443-1451.*
- *Weber T, Maier-Funk C, Ohlhauser D, Hillenbrand A, Cammerer G, Barth TF, Henne-Bruns D, Boehm BO, Reske SN, Luster M. Accurate preoperative localization of parathyroid adenomas with C-11 methionine PET/CT. Ann Surg. 2013; 257:1124-8.*



Evaluation of motion patterns by a newly developed sensor glove.

Department of Orthopedic Trauma, Hand, Plastic and Reconstruction Surgery

Head of Department: Prof. Dr. Florian Gebhard

Keywords: Computer assisted surgery | hand surgery | inflammatory response| joint replacement | Trauma surgery

The Department of Orthopedic Trauma is the second oldest of its type in Germany. It performs an average of 6,500 surgical procedures per annum and treats some 35,000 outpatients. The department is run by the Medical Director (Chair of Trauma Surgery), ten senior consultants and 26 doctors (eight female registrars and interns). The Trauma Laboratory (Prof. Dr. M. Huber-Lang) includes two PhDs, six female technicians as well as several doctoral students.

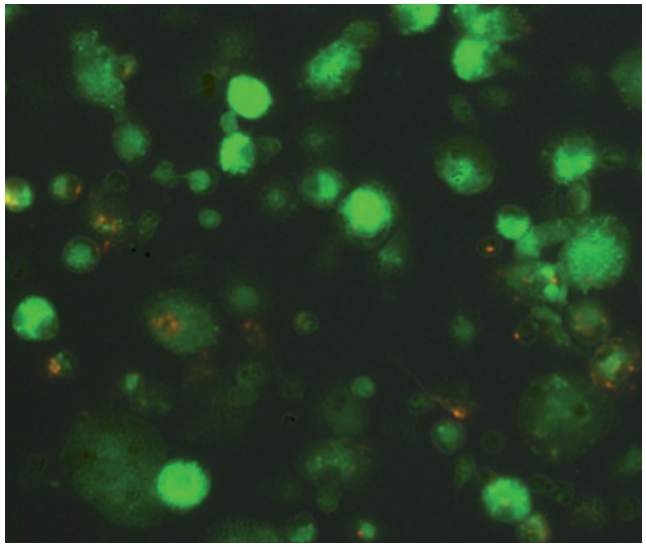
The department also incorporates the Division of Hand and Plastic Surgery (Prof. Dr. M. Mentzel). The research focus of this division concentrates on the analysis of the functional movement of the hand. In order to evaluate motion patterns, a sensor glove has been developed in cooperation with the Department of Robotics and Computational Biology at the Technical University of Berlin. This model may improve handling of a myo-electric prosthesis of the hand or help evaluate the severity of injuries and ongoing rehabilitation (Figure 1).

The Trauma Laboratory is part of the Clinical Research Unit 200 (DFG) that focuses on the inflammatory response and coagulation disorders of patients with multiple injuries. In an experimental setting, ex vivo and in vivo models have been developed to simulate multiple injuries consisting of a simultaneous head injury, chest injury, femur fracture and soft tissue injury. The aim is to elucidate the sequelae of combined injuries and to identify major factors of complications and outcome. A current and future focus also investigates the role of major co-morbidities on the molecular danger response after trauma (Figure 2).

Within the European REBORNE project on stem cells and artificial bone substitutes, the department is part of a multicenter clinical evaluation of stem cell-loaded bone allograft in delayed fracture healing and has already enrolled patients.

The multicenter study ORCHID ("Open Reduction and Fixation versus Closed Reduction in Distal Radius Fractures in the Elderly") investigated in a prospective, randomized and controlled multicenter trial, if surgical management with volar plating of intra-articular wrist fractures is superior to cast immobilization in elderly patients. The controversial results in 187 randomized patients showed that surgical management with volar plating is not significantly superior to cast immobilization in terms of health-related quality of life outcomes.

The department covers every type of fracture care by using the latest implant technologies. As a Level I trauma center, the department is part of the German Trauma Network (DGU) and has been given a rating with the highest level of trauma care (SAV Hospital DGUV). Spinal surgery is performed using 3D computer guidance, a new technology that has been clinically evaluated in recent years in the department and realized as a high-end OR. This Hybrid OR at Ulm University Hospital combines a traditional OR with a 3D robotic imaging system in combination with an integrated interface to a navigation system and complete table integration. This unique high-precision imaging in the OR may take trauma surgery to another level. Special expertise allows treatment of bone and soft tissue tumors (on average 100 cases per annum). To achieve the best individual therapy for rare tumors, each case is discussed at the CCCU.



A further specialty is the analysis of leg deformities and correction that includes intraoperative computer guidance. Posttraumatic or degenerative joint destruction is treated by replacement of the joint where, in terms of knee joint replacement, computer guidance is also used.

Alveolar macrophages (green) ingesting apoptotic alveolar epithelial type II cells (red) after blunt chest trauma

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Selected Publications:

- *Ehrnthaller C, Huber-Lang M, Nilsson P, Bindl R, Redeker S, Recknagel S, Rapp A, Mollnes T, Amling M, Gebhard F, Ignatius A. Complement c3 and c5 deficiency affects fracture healing. PLoS One. 2013 Nov 18;8(11):e81341*
- *Unnewehr H, Rittirsch D, Sarma JV, Zetoune F, Flierl MA, Perl M, Denk S, Weiss M, Schneider ME, Monk PN, Neff T, Mihlan M, Barth H, Gebhard F, Ward PA, Huber-Lang M. Changes and regulation of the C5a receptor on neutrophils during septic shock in humans. J Immunol. 2013 Apr 15;190(8):4215-25.*
- *Röderer G, Brianza S, Schiuma D, Schwyn R, Scola A, Gueorguiev B, Gebhard F, Tami A. Mechanical assessment of local bone quality to predict failure of locked plating in a proximal humerus fracture model. Orthopedics. 2013 Sep;36(9):e1134-40.*
- *Röderer G, Brianza S, Schiuma D, Schwyn R, Scola A, Gueorguiev B, Gebhard F, Tami A (2013): Mechanical assessment of local bone quality to predict failure of locked plating in a proximal humerus fracture model. Orthopedics 1;36(9):e1134-40*
- *Gebhard F, Huber-Lang M. Polytrauma--pathophysiology and management principles. Langenbecks Arch Surg. 2008 Nov;393(6):825-31.*



Department of Cardiothoracic and Vascular Surgery

Head of Department: Prof. Dr. Andreas Liebold

Keywords: Endoscopic mitral valve repair | transcatheter aortic valve implantation | endovascular aortic repair | myocardial regeneration | individualized teaching

The clinical focus of our department is keyhole surgery and percutaneous techniques as applied in a variety of heart, lung and vascular diseases. Videoscopic techniques enable mitral and tricuspid valve repair while keeping the breastbone intact. Catheter-guided percutaneous procedures are carried out in a cutting-edge hybrid suite and allow for less invasive implantation of aortic valve bioprostheses and vascular stentgrafts. Most pulmonary lesions are fixed either through videoscopy or less invasive incisions.

Key aspects of our clinical research are minimally invasive heart valve therapy, management of heart-lung machine, and alternative treatment methods of end-stage heart failure. In 2013 our department was the first center worldwide that was able to implant all catheter-based heart valves available at the time. Establishing scientific cooperation with imaging- and technology-related developers will help provide our patients with tailored treatment options in the future. Minimizing extracorporeal circuit, implementation of pulsatile perfusion and optimization of anticoagulation are subject to randomized clinical trials initiated by our department. A controlled world-wide trial investigating the effects of biopolymer injection into the failing heart has been initiated with the participation of four German centers, one of which is Ulm University.



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Applying scientific techniques of regenerative medicine to cure cardiovascular diseases is the main focus of our basic research team. In a joint project with the Department of Transfusion Medicine, the interactions between bone-marrow mesenchymal stem cells and cardiomyocytes are studied to identify signaling pathways relevant for treating myocardial ischemia and heart failure.
We study the effects of combination therapies of established and novel vasodilators in an ex vivo model of pulmonary arterial hypertension as part of a multicenter program.

In an effort to bundle individual teaching activities centered on clinically related topics, we have introduced an interdisciplinary student course focusing on organ systems (heart, lung, blood vessels). This voluntary teaching track is offered to highly motivated students with a special interest in thoracic and cardiovascular medicine.

Selected Publications:

- *Ried M, Potzger T, Neu R, Sziklavari Z, Szöke T, Liebold A, Hofmann HS, Hoenicka M: Combination of Sildenafil and Bosentan for Pulmonary Hypertension in a Human Ex Vivo Model.Cardiovasc Drugs Ther. (2013). DOI 10.1007/s10557-013-6499-0.*
- *Emini R, Wildhirt SM, Guilliard P, Brunner H, Beyer M, Liebold A: Indirect myocardial revascularization: great therapeutic potential if understanding the mechanisms. Circulation 127(1):e1-3 (2013).*
- *Lee RJ, Hinson A, Helgerson S, Bauernschmitt R, Sabbah HN. Polymer-based restoration of left ventricular mechanics. Cell Transplant. 2013;22(3):529-33.*
- *Lange R, Bleiziffer S, Piazza N, Mazzitelli D, Hutter A, Tassani-Prell P, Laborde JC, Bauernschmitt R. Incidence and treatment of procedural cardiovascular complications associated with trans-arterial and trans-apical interventional aortic valve implantation in 412 consecutive patients. Eur J Cardiothorac Surg. 2011 Apr 22.*
- *Yerebakan C, Kaminski A, Westphal B, Donndorf P, Glass A, Liebold A, Stamm C, Steinhoff G: Impact of preoperative left ventricular function and time from infarction on the long-term benefits after intramyocardial CD133(+) bone marrow stem cell transplant. J Thorac Cardiovasc Surg. Dec;142(6):1530-9 (2011).*



Division of Cardiac Anesthesiology

Head of Division: PD Dr. Helmut Reinelt

Keywords: Cardiac anesthesiology | cardiac intensive care | teaching and medical education

With the maximum experience and expertise in cardiac anesthesia and cardiac intensive care, the 16 physicians of our department guarantee the highest level of patient care and patient safety. With our high degree of specialization and our explicit dedication to patients with heart diseases, and together with our expert knowledge in anesthesiology, hemodynamic monitoring and in specific hemodynamic therapy, we have become a leading, reliable and effective contributor to modern heart surgery.

In 2013, anesthesia was performed in more than 1,000 cardiac operations with and without extracorporal circulation, including highly innovative minimally invasive procedures. Minimally invasive mitral valve repair operations, minimally invasive aortic valve replacements, minimalized extracorporal circulation system use or MIDCAB procedures are examples for high-tech-operations demanding perfect interaction and well-rehearsed teamwork of cardiac surgeons, perfusionists and cardiac anesthetists.

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In addition, we have cared for about 100 patients undergoing transaortic valve replacement (TAVI) therapy, the majority of whom had an extremely high risk profile. For this group of patients we are likewise able to offer anesthesiological care precisely suited to each patient's personal needs as well as for the requirements of a patient's health status, be it by performing general anesthesia or by safeguarding reliable analgesia in combination with a mild sedation.

Our ICU (12 beds) offers modern cardiac intensive care including intraaortic counterpulsation, continuous renal replacement and hemadsorption therapy as well as extracorporal membrane oxygenation or right- and/or left-ventricular assist devices.

For patients of a cardiac ICU the subtle balance of their coagulation status is of the utmost importance and the members of our staff are well trained in using quick and near-patient coagulation diagnostic tools as well as differentiated point-of-care testing methods such as rotation thrombelastography or platelet function testing.

To stay in close professional contact with other ICU physicians we are an active member of the Baden-Württemberg ICU peer review program that has been created as a quality assurance program in this highly challenging field of medicine.

Highlighting our commitment to medical education, our specialists are involved in postgraduate courses in TEE, CRRT, coagulation and ultrasound. In undergraduate education our course entitled "Cardiac Anesthesia," which focuses on hemodynamic monitoring and therapy for patients with heart diseases, represents one of the most favored and best evaluated courses in the elective course program of the Medical Faculty.



Selected Publications:

- *Oechsner W, Geiler S, Huber-Lang M. The impact of a dedicated training program for oral examiners at a medical school in Germany: a survey among participants from operative and non-operative disciplines. Patient Saf Surg 2013; 7(1):22.*
- *Oechsner W, Geiler S, Huber-Lang M. Effects and Sustainability of Trainings for the Oral and Practical Part of the German Final Exam in Medicine. GMS Z Med Ausbild 2013; 30(3):Doc36.*
- *Oechsner W, Boeckers A. Medical Journals as Implicit Role Models for Writing Good Multiple Choice Questions – to Which Degree Do CME-Tests Meanwhile Fulfill Formal Quality Criteria? Z Evid Fortbild Qual Gesundh wesen (ZEFQ) 2013; 107 (7):468-74.*



The Ulm hybrid OR with Artis zeego angiography.

Department of Neurosurgery

Head of Department: Prof. Dr. Christian Rainer Wirtz

Keywords: Intraoperative Imaging | Neurooncology | Peripheral Nerve Surgery | Traumatic Brain Injury | Vascular Surgery| Plexus Surgery | Pediatric Neurosurgery

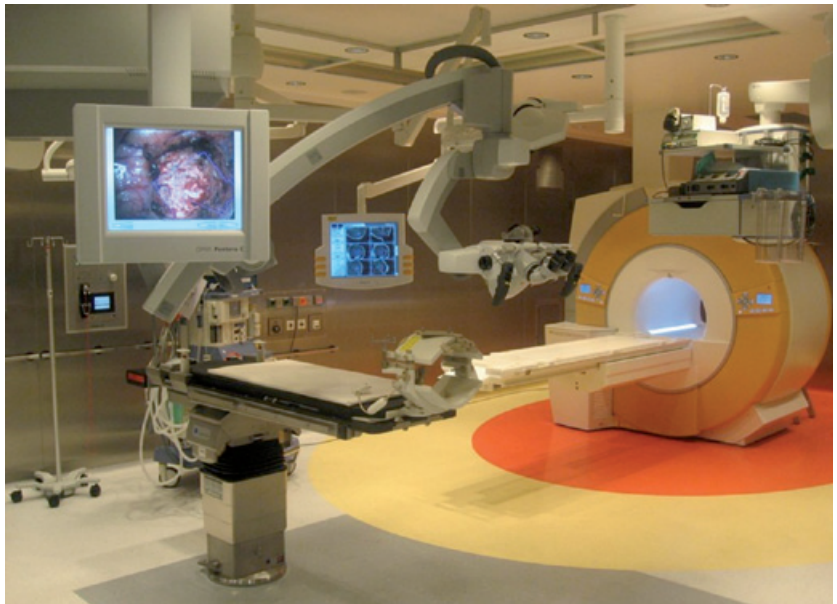
The Department of Neurosurgery at Ulm University is headed by Professor Wirtz and is now one of the largest neurosurgical units in Germany. Twelve neurosurgeons and 13 residents provide outpatient care to more than 9,000 patients from around the world and perform more than 3,500 neurosurgical procedures each year. The team that includes eight women and five members from abroad is proud to cooperate with colleagues in other disciplines to offer expertise in treating a wide range of neurological and neurosurgical conditions. They are aided by outstanding and highly-skilled support staff. Our team of neurosurgeons provides thorough examinations, diagnoses and treatments for brain, nerve, and spinal cord diseases and disorders in children and adults. Each patient is treated individually since physical, psychological and cultural differences may affect treatment choices.

The Department of Neurological Surgery at Ulm University has two locations, namely, Ulm (State of Baden-Württemberg) and Günzburg (Federal State of Bavaria) with a total of 99 beds that includes intensive and intermediate care as well as normal ward units for adults and children.
Our facilities include cutting-edge equipment, i.e. modern surgical microscopes (including 5-ALA fluoromicroscopy and intraoperative infrared angiography), image-guided brain and spine navigation tools as well as monitoring techniques. Furthermore, we offer two of the most advanced neurosurgical theaters in Europe, the BrainSuite©, which combines state-of-the-art neuronavigation and intraoperative magnetic resonance technology (Magnetom Espree® 1.5 Tesla) in Günzburg and an intraoperative angiography hybrid OR (Artis Zeego (c)) in Ulm, for the benefit of patients with a variety of conditions.

Our physicians are leaders in their field and contribute to advancements in brain, spine, endovascular and operative neurovascular surgery, neurotraumatology, pediatric neurosurgery and peripheral nerve care. Our goal is to provide optimal care to patients with neurological disorders and to enhance it through the continuous incorporation of advancing scientific knowledge. Our research efforts in neurovascular surgery, neuronavigation and tumor biology aim to break new scientific grounds that are relevant to neurosurgical practice.

Focused on brain surgery, peripheral nerve surgery, cerebrovascular concepts as well as neurotraumatology, our resident teaching programs are designed to promote a profound understanding of neurological surgery and to inspire patient care by fostering technical and surgical skills and by encouraging scientific inquiry.

The daily neurosurgical routine includes the training of medical students with an emphasis on practical bedside teaching. Training is offered either as a standard part of a student's curriculum or by individual appointment. We encourage students interested in the neurological and neurosurgical field to complete their dissertation in our department.



BrainSuite© panorama, Günzburg

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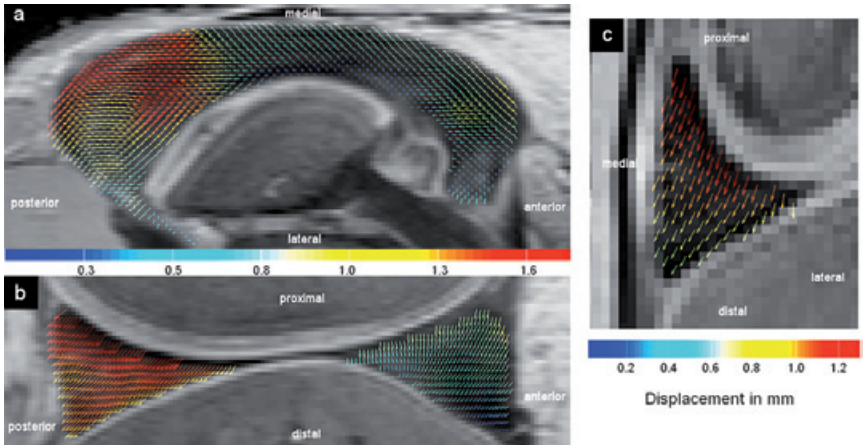
Selected Publications:

- *Karpel-Massler G, Westhoff MA, Zhou S, Nonnenmacher L, Dwucet A, Kast RE, Bachem MG, Wirtz CR, Debatin KM, Halatsch ME: Combined inhibition of HER1/EGFR and RAC1 results in a synergistic antiproliferative effect on established and primary cultured human glioblastoma cells. Mol Cancer Ther 2013 Sep;12(9):1783-95.*
- *Tjahjadi M, Heinen C, König R, Rickels E, Wirtz CR, Woischneck D, Kapapa T: Health-related quality of life after spontaneous subarachnoid hemorrhage measured in a recent patient population. World Neurosurg 2013 Feb;79(2):296-307.*
- *Cubital tunnel syndrome - a review and management guidelines. Assmus H, Antoniadis G, Bischoff C, Hoffmann R, Martini AK, Preissler P, Scheglmann K, Schwerdtfeger K, Wessels KD, Wüstner-Hofmann M. Cent Eur Neurosurg. 2011 May;72(2):90-8.*
- *König RW, Heinen CP, Antoniadis G, Kapapa T, Pedro MT, Gardill A, Wirtz CR, Kretschmer T, Schmidt T: Image guided aneurysm surgery in a Brainsuite® ioMRI Miyabi 1.5 T environment. Acta Neurochir Suppl. 2011;109:107-10.*
- *Coburger J, König R, Seitz K, Bäzner U, Wirtz CR, Hlavac M. Determining the utility of intraoperative magnetic resonance imaging for transsphenoidal surgery: a retrospective study. J Neurosurg. 2013, published online December 13, 2013; DOI: 10.3171/2013.9.JNS122207.*



Displacement vectors of the meniscus under axial knee joint loading calculated from MRI images.

Institute of Orthopedic Research and Biomechanics

Head of Institute: Prof. Dr. Anita Ignatius

Keywords: Bone regeneration | biomaterials | fracture healing | joint biomechanics | spine biomechanics

The Institute of Orthopedic Research and Biomechanics performs basic and translational research on the pathophysiology and treatment of musculoskeletal disorders. An interdisciplinary research team of 40 engineers, biologists, molecular biologists, physicians and veterinarians work closely together (four professors, seven postdocs, sixteen PhD students, eleven technicians, two employees from abroad; of these 68% are female).

Our scientific work focuses on five main fields: fracture healing and bone regeneration; biomaterials and tissue engineering; cell biology; and joint as well as spine biomechanics.

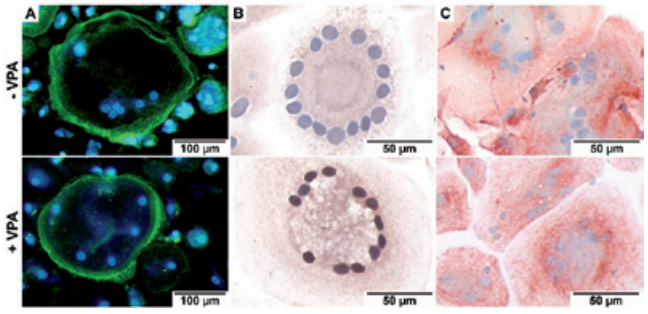
In the field of bone healing, the major goals are to increase the knowledge of the complex regeneration process itself and to improve the treatment of bone fractures. As bone regeneration significantly depends on mechanical factors, we are interested in the underlying mechanisms. Furthermore, we are interested in delayed healing associated with osteoporosis or inflammatory processes. We are currently a part of two DFG-funded research groups (FOR793, KFO200) dealing with the subjects of “Mechanisms in Fracture Healing and Bone Regeneration in Osteoporosis” and “Inflammatory Response after Musculoskeletal Trauma.”

There is an increasing demand for biomaterials to treat or replace injured or diseased tissues. In the biomaterial research group we investigate bone, ligament and intervertebral disc replacement materials with a focus on degradable materials since these increase the chances of a complete recovery. Several of our projects deal with the development of “smart,” that is, structurally or biologically functionalized materials that allow specific control of cell function.

The aim of the cell biology group is to investigate the mechanisms of mechanotransduction in cells of the musculoskeletal system since regeneration and remodeling are strictly influenced by mechanical load. The involved pathways are of great interest because they can be possible targets for therapeutic intervention in regenerative therapies. Furthermore, we also investigate the interaction of cells with biomaterials. In EU-funded projects, we focus on the investigation of cellular changes in intervertebral disc degeneration and regeneration strategies.

The focus of the joint biomechanics research group is related to clinically relevant issues of the large joints. Cruciate ligament and meniscus surgery as well as total joint arthroplasty are of special interest. Biomechanical in vitro tests, finite-element modeling and in vivo functionality testing of implants are part of the scope of our research group.

The spine research team applies state-of-the-art in vitro and in vivo methods as well as finite-element models for basic research regarding spine biomechanics to gain a better understanding of loading and motions of the spine. The goal is to develop methods of diagnosis and evaluate treatment procedures in addition to regenerative strategies to improve and test spinal implants for the surgical treatment of spinal injuries, disc degeneration, and osteoporotic fractures and deformities.



Actin ring formation, calcitonin receptor expression and osteoclast specific vacuolar proton pump subunit TCIRG1 expression of osteoclasts.

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Selected Publications:

- *Heilmann A, Schinke T, Bindl R, Wehner T, Rapp A, Haffner-Luntzer M, Nemitz C, Liedert A, Amling M, Ignatius A. (2013) The Wnt Serpentine Receptor Frizzled-9 Regulates New Bone Formation in Fracture Healing. PLoS One 31;8(12):e84232.*
- *Reitmaier S, Schmidt H, Ihler R, Kocak T, Graf N, Ignatius A, Wilke HJ. (2013) Preliminary investigations on intradiscal pressures during daily activities: an in vivo study using the merino sheep. PLoS One 24;8(7):e69610.*
- *Claes L, Recknagel S, Ignatius A (2012) Fracture healing under healthy and inflammatory conditions. Nat Rev Rheumatol 31;8(3):133-43*
- *Tautzenberger A, Kreja L, Zeller A, Lorenz S, Schrezenmeier H, Mailänder V, Landfester K, Ignatius A. (2011) Direct and indirect effects of functionalised fluorescence-labelled nanoparticles on human osteoclast formation and activity. Biomaterials 32(6):1706-14.*
- *Dürselen L, Vögele S, Seitz AM, Ignatius A, Friederich NF, Bauer G, Majewski M (2011) Anterior Knee Laxity Increases Gapping of Posterior Horn Medial Meniscal Tears. Am J Sports Med 39 (8):1749-1755.*



Students practicing endotracheal intubation during induction of anesthesia using the patient simulator.

Department of Anesthesiology

Head of Department: Prof. Dr. Dr. h.c. Michael Georgieff

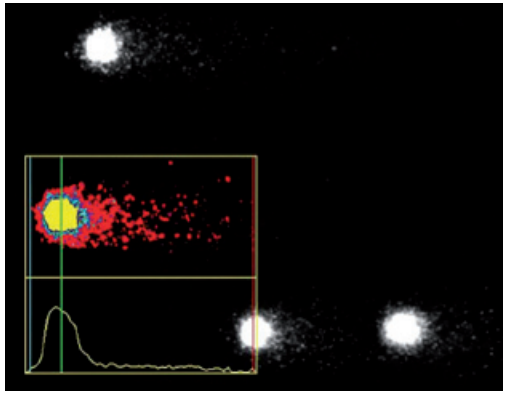
Keywords: Biomarker profiling | breath tests | investigational animal intensive care unit | oxidative stress | stable, non-radioactive isotope

The Department of Anesthesiology employs a staff of 99 MDs (40 % female) and is in charge of the perioperative care of all surgical disciplines. In addition to the main clinical department responsible for patients from the Departments of Orthopedic, Trauma and Plastic Surgery, Vascular and Thoracic Surgery and Visceral Surgery, it comprises four clinical divisions: the Division of Special Anesthesiology (Head: PD Dr. med. Wolfram Schütz) responsible for the clinical care of ear, nose and throat, gynecology and obstetrics, ophthalmology and urology patients; the Division of Emergency Medicine (Head: Prof. Dr. med. Claus-Martin Muth) in charge of all emergency cases in the city of Ulm and surrounding districts; the Division of Operative Intensive Care (Head: PD Dr. med. Eberhard Barth) responsible for all surgical disciplines; and the Division of Pain Therapy (Head: PD Dr. med. Peter Steffen) which takes care of all perioperative pain management and chronic pain patients. Approximately 34.000 patients are treated each year. The department organizes the Medical School's teaching in emergency medicine, anesthesia and perioperative care, disaster medicine and diving as well as hyperbaric medicine, and participates in numerous other courses in medicine and molecular medicine. In addition, it is responsible for the training of "standardized patients" by recruiting actors as well as employing the use of high-end patient-simulators, and thus has the largest teaching activity of all the clinical departments of the Medical Faculty. All student examinations are organized as *Objective Structured Clinical Evaluations (OSCE)*.

The department comprises two research divisions:

1. Division of Experimental Anesthesiology (Head: Prof. Dr. rer. nat. Elisabeth Marion Schneider) The main scientific topics are single nucleotide polymorphisms, biomarker profiling, and the role of the nuclear transcription factor-kB in patients with sepsis and hemophagocytic diseases. Ion channel effects of anesthetics are evaluated using patch-clamp techniques.

2. Division of Pathophysiology and Process Development in Anesthesia (Head: Prof. Dr. med. Dr. h.c. Peter Radermacher) The main scientific topics are: the role of various gaseous mediators such as NO, CO, H2S, and O2 during circulatory shock of various etiologies; the pre-clinical evaluation of innovative treatments under these conditions; the quantification of whole body and organ-specific metabolic pathways using stable and non-radioactive labeled isotopes in blood and breath tests and the determination of the activity of the complexes of the mitochondrial respiratory chain under various conditions. For this purpose, unique porcine and murine “investigational intensive care units” have been established to allow clinically relevant experimental models. Together with the Division of Emergency Medicine, research activity is applied to human physiology research during diving and hyperbaric conditions as well as to emergencies under special environmental conditions e.g. cold and drowning.



Nuclei with marked oxidative DNA damage as assessed using single cell gel electrophoresis (alkaline comet assay) in isolated lymphocytes exposed to hyperbaric oxygen.

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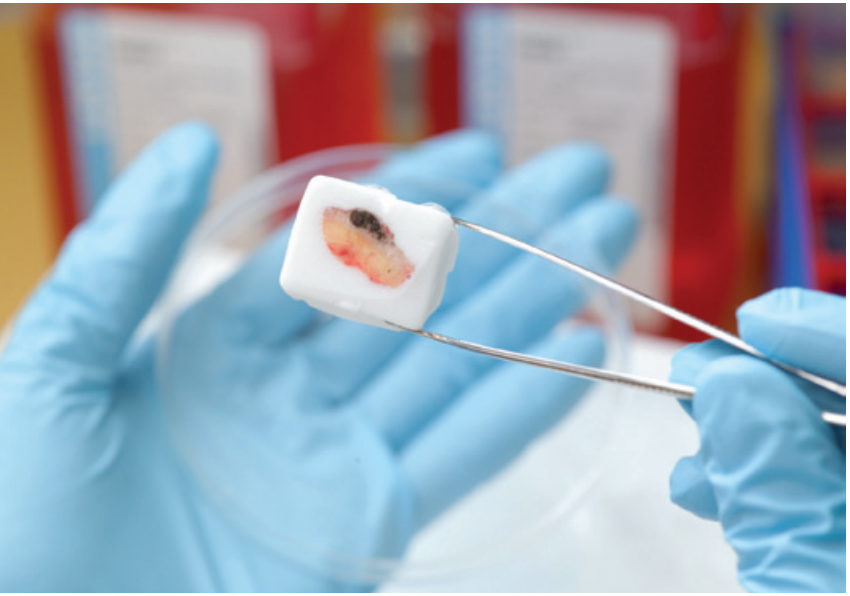
Selected Publications:

- *Matějková S, Scheuerle A, Wagner F, McCook O, Matallo J, Gröger M, Seifritz A, Stahl B, Vcelar B, Calzia E, Georgieff M, Möller P, Schelzig H, Radermacher P, Simon F (2013) Carbamylated erythropoietin-FC fusion protein and recombinant human erythropoietin during porcine kidney ischemia/reperfusion injury. Intensive Care Med 39:497-510.*
- *Winkler BE, Eff AM, Eff S, Ehrmann U, Koch A, Kähler W, Muth CM (2013) Efficacy of ventilation and ventilation adjuncts during in-water-resuscitation--a randomized cross-over trial. Resuscitation 84:1137-1142.*
- *Bracht H, Scheuerle A, Gröger M, Hauser B, Matallo J, McCook O, Seifritz A, Wachter U, Vogt JA, Asfar P, Matejovic M, Möller P, Calzia E, Szabó C, Stahl W, Hoppe K, Stahl B, Lampl L, Georgieff M, Wagner F, Radermacher P, Simon F (2012) Effects of intravenous sulfide during resuscitated porcine hemorrhagic shock. Crit Care Med 40:2157-67*
- *Wagner F, Scheuerle A, Weber S, Stahl B, McCook O, Knöferl MW, Huber-Lang M, Thomas J, Asfar P, Szabó C, Möller P, Gebhard F, Georgieff M, Calzia E, Radermacher P, Wagner K (2011) Cardiopulmonary, histological and inflammatory effects of intravenous H2S after blunt chest trauma-induced lung contusion in mice. J Trauma 71:1659-1667.*
- *Schneider EM, Du W, Fiedler J, Högel J, Günther KP, Brenner H, Brenner RE (2011) The (-765 G→C) promoter variant of the COX-2/PTGS2 gene is associated with a lower risk for end-stage hip and knee osteoarthritis. Ann Rheum Dis 70:1458-1460.*



Histologic techniques help to understand the pathogenesis of malignant melanoma and other skin diseases.

Department of Dermatology and Allergology

Head of Department: Prof. Dr. Karin Scharffetter-Kochanek

Keywords: Aging | allergy | autoimmunity | dermatology | melanoma | stem cells | wound healing

Our department's mission is sustained leadership in patient care, in clinical and basic research, and in educating leaders of dermatology and allergology in an environment that fosters creativity, excellence and synergy. Dermatology in general, and dermatology at Ulm University in particular, has undergone an impressive development from descriptive morphology to understanding pathomechanisms with systemic and targeted therapies. An intensive program aimed at education, research and patient service has been established at the department with the focus on allergy, autoimmune and inflammatory diseases, wound disorders and regenerative medicine, malignancies, aging, and infectious disorders of the skin. The department offers fully accredited postgraduate training with Board Certification. Research goals are to explore mechanisms of skin biology and to gain insights into aging, inflammatory diseases, skin tumors and wound healing. Our research is organized in part within the Clinical Research Group KFO142 ("Molecular and cellular aging – from mechanisms to clinical perspectives"), the Research Training Group GRK1789 (CEMMA – "Cellular and Molecular Mechanisms in Aging"), and the Research Nucleus SyStaR ("Molecular Systems Biology of impaired stem cell function and regeneration during aging"). Funded clinical studies comprise targeted tumor therapies and allergies in the elderly. Major research topics and/or clinical foci include: skin aging and related diseases; immunosenescence and adaptive immunity; progeroid syndromes; stem cells and their niches in aging and regeneration including wound repair and skin carcinogenesis. More recently, we have established research lines for aging-related diseases including the molecular dissection of mechanisms underlying type I allergies in the elderly (ATOPICA),

chronic non-healing wounds in the elderly, and the senescence-associated secretory phenotype of senescent fibroblasts driving melanoma progression. Our thematic foci in research are reflected in our clinical specialization. Accordingly, our clinic has been certified and accredited as a Center of Excellence for Allergic Diseases (*Global Allergy and Asthma European Network*) and Skin Tumors (*Hauttumorzentrum*). In addition, we have been accredited as a center specializing in diagnostics and the care of patients suffering from wound healing disorders (*Wundsiegel*). Our specific clinical focus is on inflammatory skin diseases and complex autoimmune disorders (e.g. psoriasis, atopic dermatitis and contact dermatitis, lupus erythematodes, scleroderma and dermatomyositis), skin tumors as well as on wound healing disturbances with the goal of enhancing the interdisciplinary quality of patient care and therapy. Recently we have established a Center for Extracorporal Photopheresis (ECP). The ECP technique employing three running machines has been developed to successfully treat graft-versus-host disease after stem cell transplantation. The continuous support of our entire community consisting of the faculty, patients, friends and alumni will be instrumental in providing the resources needed to support trainees, the junior faculty, advances in patient care and original research in the future.



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Selected Publications:

- *Gonzalez OG, Assfalg R, Koch S, Schelling A, Meena JK, Kraus J, Lechel A, Katz SF, Benes V, Scharffetter-Kochanek K, Kestler HA, Günes C, Iben S. (2014): Telomerase stimulates ribosomal DNA transcription under hyperproliferative conditions. Nat Commun. 5:4599-610.*
- *Qi Y, Jiang D, Sindrilaru A, Stegemann A, Schatz S, Treiber N, Rojewski M, Schrezenmeier H, Vander Beken S, Wlaschek M, Böhm M, Seitz A, Scholz N, Dürselen L, Brinckmann J, Ignatius A, Scharffetter-Kochanek K. (2014): TSG-6 Released from Intradermally Injected Mesenchymal Stem Cells Accelerates Wound Healing and Reduces Tissue Fibrosis in Murine Full-Thickness Skin Wounds. J Invest Dermatol. 134:526-537.*
- *Florian MC, Nattamai KJ, Dörr K, Marka G, Uberle B, Vas V, Eckl C, Andrä I, Schiemann M, Oostendorp RA, Scharffetter-Kochanek K, Kestler HA, Zheng Y, Geiger H. (2013): A canonical to non-canonical Wnt signalling switch in haematopoietic stem-cell ageing. Nature. 503: 392-6.*
- *Gatzka M, Hainzl A, Peters T, Singh K, Tasdogan A, Wlaschek M, Scharffetter-Kochanek K. (2013): Reduction of CD18 Promotes Expansion of Inflammatory γδ T Cells Collaborating with CD4+ T Cells in Chronic Murine Psoriasiform Dermatitis. J Immunol. 191:5477-88.*
- *Jiang D, Qi Y, Walker N, Sindrilaru N, Hainzl A, Wlaschek M, MacNeil S, Scharffetter-Kochanek K. (2013): The Effect of Adipose Tissue Derived MSCs Delivered by a Chemically Defined Carrier on Full-Thickness Cutaneous Wound Healing. Biomaterials 34:2501-15.*

Department of Gynecology and Obstetrics

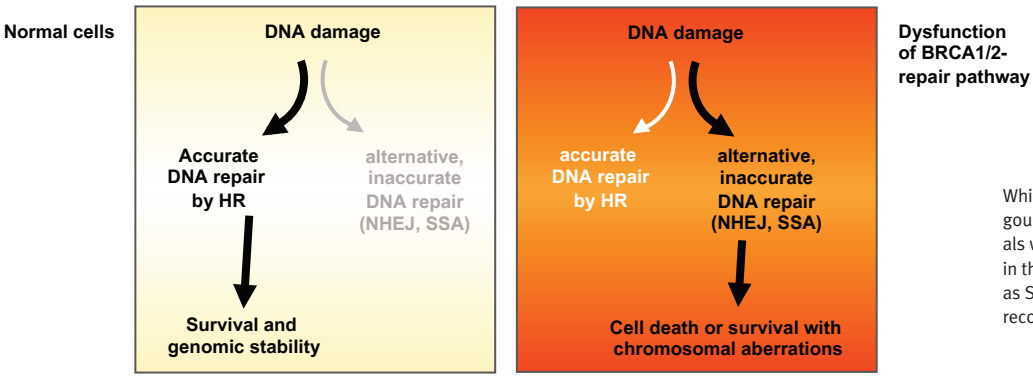
Head of Department: Prof. Dr. Wolfgang Janni

Keywords: Biomarkers | Cancer Susceptibility | Angiogenesis | BRENDA | DNA repair

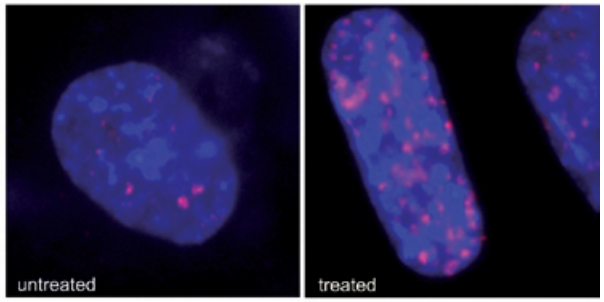
The scientific projects were supported by the BMBF, DFG, German Cancer Aid, Sander Foundation and Alexander von Humboldt Foundation.

Biomarkers for Cancer Susceptibility

Algorithm-based pedigree and candidate gene analyses are the pillars for the identification of breast and ovarian cancer risk to license intensive care programs. Considering the demographic development and the fact that predisposing mutations explain less than a third of the risk, new research avenues were taken. Because most risk genes are linked with DNA repair deficiencies, a corresponding test system was developed for primary cells from patient samples (EP1399576). Analysis of cells with defined risk genes revealed a functional signature as a potential phenotypic biomarker. The first case-control study for prospective evaluation of this signature was based on the BMBF-funded BRENDA platform and revealed association with familial risk. Importantly, this biomarker captures various defects and thus exceeds the limits of genotyping.



While normal cells preferentially use the accurate HR (homologous recombination) DNA repair pathway, cells from individuals with hereditary breast cancer risk, such as due to a defect in the BRCA1/2 pathway, shift to inaccurate pathways such as SSA (single-strand annealing) and NHEJ (non-homologous recombination) resulting in chromosomal aberrations.



Epithelial cells from a breast cancer specimen were subjected to radiomimetic treatment *ex vivo* and DNA damage markers (red) in the nucleus (blue) as visualized by immunofluorescence microscopy.

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Angiogenesis and the Ovarian Hyperstimulation Syndrome

Hormonal stimulation by hCG was found to increase VEGF levels followed by downregulation of adhesion proteins and thus increased permeability. Comparable mechanisms were discovered in ovarian cancer for the first time unveiling the pathomechanism of ascites production.

Student Education

In addition to lectures, students are trained in a one-week clinical rotation to gain insight into the processes of our outpatient clinic, ultrasound department, surgery rooms and labor ward. A skills laboratory with breast and pelvic examination models as well as a laparoscopic surgery training model and a sophisticated delivery trainer (Noelle) are employed. In addition, we offer voluntary courses for advanced students, ranging from interdisciplinary breast cancer to assisted reproductive techniques and intensified obstetric training. Clinical rotations (2-6 weeks) are well established for national and international students and a two-day revision course supports our students before the final exam.

Selected Publications:

- *Deniz, M, Holzmann, K, Wiesmüller, L. (2013). Functional Analysis – Make or break for cancer predictability. Mutat. Res. 743-744:132-141.*
- *Varga, D, Deniz, M, Schwentner, L, Wiesmüller, L. (2013). Ovarian Cancer: in search of better marker systems based on DNA repair defects. Int J Mol Sci 14, 640-673.*
- *Böhringer, M, Obermeier, K, Griner, N, Waldraff, D, Dickinson, E, Eirich, K, Schindler, D, Hagen, M, Jerry, D.J, Wiesmüller, L. (2013). siRNA screening identifies differences in the Fanconi anemia pathway in BALB/c-Trp53+/- with susceptibility versus C57BL/6-Trp53+/- mice with resistance to mammary tumors. Oncogene 32:5458-5470.*
- *Keimling, M, Deniz, M, Varga, D, Stahl, A, Schrezenmeier, H, Kreienberg, R, Hoffmann, I, Koenig, J, Wiesmüller, L. (2012). The power of DNA double-strand break (DSB) repair testing to predict breast cancer susceptibility. FASEB J. 26, 2094-2104.*
- *Keimling, M, Volcic, M, Csernok, A, Wieland, B, Dörk, T, Wiesmüller, L. (2011). Functional characterization connects individual patients´ mutations in Ataxia Telangiectasia Mutated (ATM) with dysfunction of specific DNA double-strand break repair signalling pathways. FASEB J. 25, 3849-3860.*



Inpatient and outpatient clinic are closely connected and provide a continuous patient support by specialists for different neurological disorders.

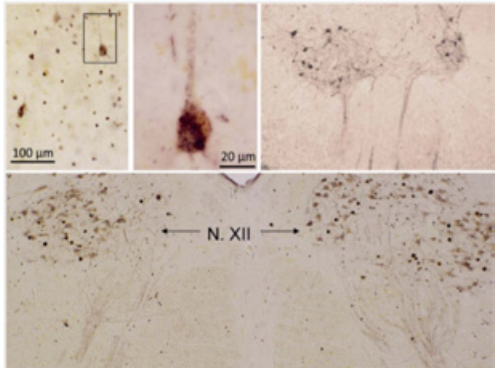
Department of Neurology

Head of Department: Prof. Dr. Albert C. Ludolph

Keywords: Biomarker Assessment | Center for Clinical Studies | Databanking | Motor Neuron Diseases | Neurodegenerative Diseases

The Department of Neurology is comprised of an inpatient clinic (*Rehabilitations- und Universitätskliniken Ulm, RKU*) and an outpatient clinic. The inpatient clinics integrate compassionate care with state-of-the-art research in general neurology and specialized areas. Our expert subspeciality care is aided by advanced diagnostic procedures that include 24/7 availability of MRI, the department's own CSF- and histological laboratory for muscle biopsies. We offer acute and rehabilitation facilities with an intensive care unit and a 27-patient stroke unit/ intermediate care unit, with 24/7 availability for the full spectrum of modern stroke therapies. The specialized outpatient clinics are headed by renowned experts in the field and cover motor neuron/ neuromuscular disorders, movement disorders such as Parkinson's and Huntington's disease, inflammatory CNS diseases, dementias, epilepsy, pain, and neurooncology. Besides serving as a specialized teaching and training center, the Center for Clinical Studies includes a large biobank. The center allows access to cutting-edge therapies and is fully financed by external sources as well as being an active partner in national and international networks.

Experimental neurology covers a broad spectrum of basic and clinical neurological research. The Neurophysiology Section focuses on neurophysiological assessment of oculomotor/vestibular functions together with functional neuroimaging and clinical Neuroophthalmology. The group for clinical neuroanatomy works on the neuropathological assessment of neurodegenerative diseases and, in 2013, added a novel neuropathological staging system for other neurodegenerative diseases, i.e. ALS and frontotemporal dementias, to their former groundbreaking staging systems in Parkinson's and Alzheimer's disease. Further subunits are the groups for synucleinopathies, for cell biology and in vivo models of ALS/MND, for molecular mechanisms of ALS, for striatal degenerations, and neuroinflammation. Topics of research are Alzheimer's disease, frontal dementias and CSF-based proteomics/biomarker, CSF diagnostics, and experimental



1. In sporadic ALS, TDP-43 pathology develops in Betz pyramidal cells of layer Vb in the primary motor cortex (upper left photo): Detail (upper middle photo) shows a single Betz cell at high resolution with pTDP-43 aggregates in the somatodendritic compartment and in unmyelinated initial portions of the axon. The pathology also develops in spinal cord ventral horn (upper right photo) alpha-motoneurons of layer 9 and in dendrites and axons heading toward the ventral root.

Lower photo: Bilateral pathology in axons and cell bodies of motor neurons of the hypoglossus nucleus (N. XII) in the lower brainstem.

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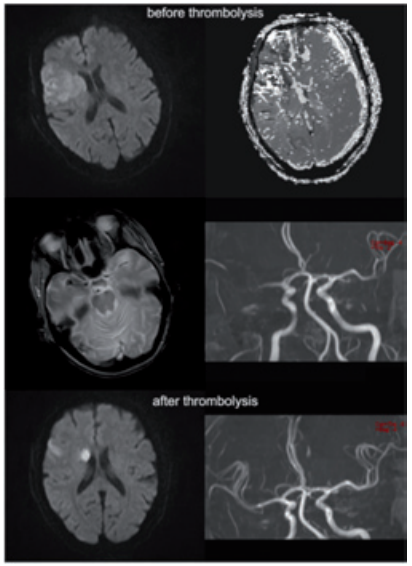
neuropsychology. All these research groups participate in the Academic Neuroscience Center Ulm (NCU) and cooperate closely with other NCU members and core facilities, in addition to a multitude of external network partners, e.g. CNS Research Boehringer-Ingelheim, and international academic neuroscience centers.

We provide a rigorous teaching concept for medical students that includes various clinical courses (including Neuro-TRACK) and a structured teaching program for the Practical Year (Teaching Bonus of the University in 2013).



2. MRI with 24/7 availability as our standard diagnostic imaging tool in acute ischemic stroke; as an example MRI-stroke imaging before and after intravenous thrombolysis in combination with mechanical recanalization.

Upper panel: before therapy, diffusion-weighted imaging (DWI) of the ischemic stroke (a) with a diffusion-perfusion-mismatch in perfusion-weighted imaging (b) due to a thrombus in the right middle cerebral artery (MCA) in T2* weighted imaging (c) and occlusion of the right MCA in TOF-angiography (d).

Lower panel: after therapy, reduction of the ischemic tissue in DWI (e) after successful recanalization of the MCA (f).

Selected Publications:

- *Braak H, Brettschneider J, Ludolph AC, Lee VM, Trojanowski JQ, Del Tredici K. Amyotrophic lateral sclerosis-a model of corticofugal axonal spread. Nat Rev Neurol. 2013;9(12): 708-14.*
- *Brettschneider J, Del Tredici K, Toledo JB, Robinson JL, Irwin DJ, Grossman M, Suh E, Van Deerlin VM, Wood EM, Baek Y, Kwong L, Lee EB, Elman L, McCluskey L, Fang L, Feldengut S, Ludolph AC, Lee VM, Braak H, Trojanowski JQ. Stages of pTDP-43 pathology in amyotrophic lateral sclerosis. Ann Neurol. 2013;74(1):20-38.*
- *Eschbach J, Schwalenstöcker B, Soyal SM, Bayer H, Wiesner D, Akimoto C, Nilsson AC, Birve A, Meyer T, Dupuis L, Danzer KM, Andersen PM, Witting A, Ludolph AC, Patsch W, Weydt P. PGC-1α is a male-specific disease modifier of human and experimental amyotrophic lateral sclerosis. Hum Mol Genet. 2013;22(17):3477-84.*
- *Stockmann M, Linta L, Föhr KJ, Boeckers A, Ludolph AC, Kuh GF, Udvardi PT, Proepper C, Storch A, Kleger A, Liebau S, Boeckers TM. Developmental and Functional Nature of Human iPSC Derived Motoneurons. Stem Cell Rev 2013;9(4):475-92*



Department of Ophthalmology

Head of Department: Prof. Dr. Gerhard K. Lang

Keywords: Age-related macular degeneration and diabetic retinopathy | ophthalmic surgery | ophthalmology

The Department of Ophthalmology covers the entire spectrum of surgical and medical ophthalmology. With a team of 25 physicians, we treated 3,272 inpatients and 23,063 outpatients in 2012, during which eight fellows from other countries and about 20 students worked in our department.

Ophthalmic surgery in the department mainly focuses on cataract, vitreoretinal surgery, glaucoma, lid surgery, refractive surgery as well as penetrating and lamellar keratoplasty (DMEK). In the area of non-surgical ophthalmology, the section for medical retina focuses on retinal vascular diseases, diabetic retinopathy and age-related macular degeneration, and provides diagnostic procedures and treatment. Retinal laser surgery, photodynamic therapy as well as intravitreal injections (IVOM) are also performed. In the area of medical, clinical and basic retina research, the focus is on age-related macular degeneration and diabetic retinopathy (Heads: Prof. Gabriele E. Lang; Dr. Heidrun Deißler). A daily morning conference, noontime case presentations in the clinic and daily rounds on the inpatient floors in addition to a weekly advanced training conference all contribute to a consistent and high level of education. An ocular pathology conference and case readout take place once a week.

As a university hospital we consider it our duty to improve and expand our achievements by employing the latest research data and technology in diagnostics and treatment. Since the establishment of the Department of Ophthalmology, the entire team of doctors has continuously sought to provide optimal treatment for our patients.



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Our efforts are regularly monitored by external questionnaires (PICKER-study 2004 and 2007) to evaluate patient satisfaction. An external questionnaire on health insurance schemes published in 2009 confirmed the achievement of our goals.

In the area of general satisfaction concerning results of treatment, nursing care as well as information and communication, our department scored 4-7 % above average among all participating departments.

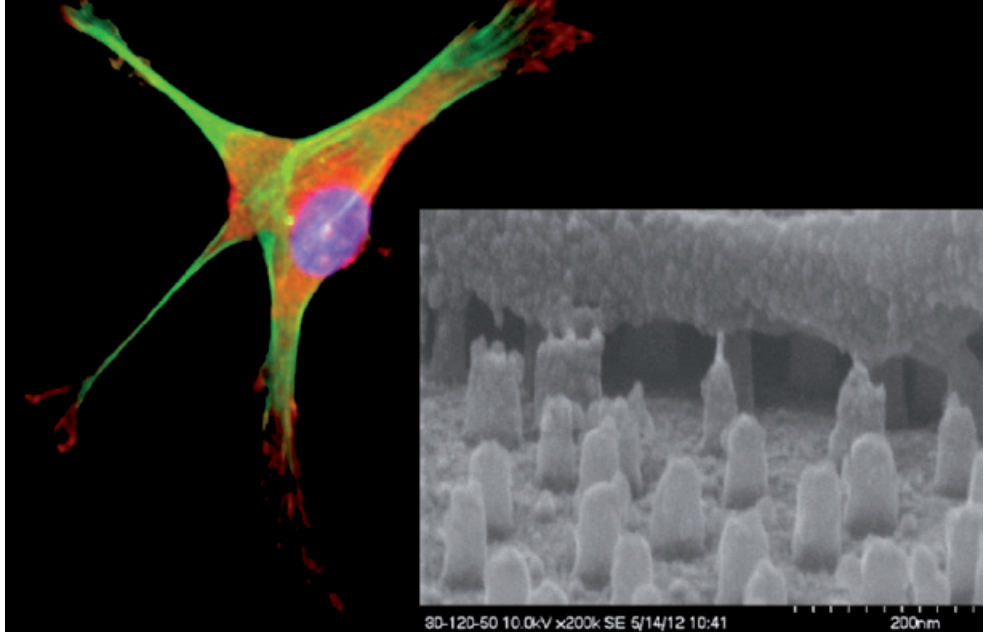
The successful certification of patient care, teaching and research according to ISO 9001 was confirmed in 2013 in an external audit.

The residency program has a certification in line with the European Board of Ophthalmology regulations.

Our most important aim is the optimum care of our patients according to the highest standards and within a pleasant atmosphere. The results have so far been extremely satisfying and it is our intention to continue in this vein.

Selected Publications:

- *Lang GE, Berta A, Beldem BM, Simader C, Sharp D, Holz FG, Sutter F, Gerstner O, Mitchell P, RESTORE extension study group. Two year safety and efficacy of Ranibizumab 0.5 mg in diabetic macular edema: interim analysis of the RESTORE extension study. Ophthalmology, 2013; 120: 2004-2012.*
- *Lang GE. Mechanismen retinaler Neurodegeneration als Folge von Diabetes mellitus. Klin Monatsbl Augenheilk 2013, 230: 929-931.*
- *Deissler HL, Deissler H, Lang, GK, Lang GE: VEGF but not PlGF disturbs the barrier of retinal endothelial cells. Experimental Eye Research 2013; 25:162-171.*
- *Deissler HL, Deissler H, Lang GE. Actions of bevacizumab and ranibizumab on microvascular retinal endothelial cells: similarities and differences Br J Ophthalmol. 2012, 96: 1023-1028.*
- *Kampmeier J, Rau T, Liebhardt H, Fegert JM, Lang GK. Adoption of OSCE Examination Procedures in Ophthalmology Klin Monatsbl Augenheilkd 2011; 228: 550–554.*



Multicolor fluorescence imaging (cytoskeleton and focal adhesions) of a mesenchymal stem cell grown on a nanopillar surface (left) and scanning electron microscopy of cell adhesion on top of the nanostructures (insert, magnification x 200.000).

Department of Orthopedics

Head of Department: Prof. Dr. Heiko Reichel

Keywords: Adult Reconstruction and Joint Replacement | Molecular Orthopedics | Orthopedic Oncology | Pediatric Surgery | Spine Surgery | Sports Medicine

The Department of Orthopedic Surgery at the RKU is one of the largest orthopedic university institutions in Germany and covers all aspects of musculoskeletal diseases, including in- and outpatient surgical and non-operative care, as well as orthotics and prosthetics. More than 3,500 surgical procedures are performed annually and about 13,000 patients are seen in our Outpatient Department. The wards, with a total of over 150 beds, include a special unit for spinal cord injury and a day clinic for a multidisciplinary musculoskeletal pain program. Before surgery, conservative treatment options are always taken into account. If the conservative approach fails to restore an acceptable level of function and to decrease pain, up-to-date procedures are performed. We guide patients through the various stages of their disease by diagnosis, treatment and rehabilitation.

Different subspecialities focus on total joint replacements of hip, knee and shoulder joints as well as elbow and ankle joints, joint reconstruction, spine surgery, pediatric orthopedics, sports medicine, orthopedic oncology and orthopedic rheumatology. On referral, septic and revision surgery is another option. In some cases, fractures of the extremities and the spine are also treated. Modern trends lead to smaller incisions (minimal-invasive surgery), computer-aided implantation of joint replacements (navigation) and to bone-preserving implants. The best treatment of the individual is

guaranteed by the selection of the most appropriate procedure and the optimized implant. Research activities focus on biomechanical aspects (development and testing of joint and spinal implants) and molecular biological and biochemical techniques in bone and soft-tissues. Several dissertations and “Habilitations” have been conducted at our Institute. The teaching of our students and residents together with an international instructional course in spine surgery are additional academic activities.

Important cooperation is maintained with the Department of Traumatology (Head: Prof. Dr. F. Gebhard), the CCCU (Comprehensive Cancer Center Ulm) and the Institute of Orthopedic Research and Biomechanics (Head: Prof. Dr. Anita Ignatius).

The Orthopedic Department incorporates the division for Biochemistry of Joint and Connective Tissue Diseases (Head: Prof. Dr. Rolf Brenner). This division concentrates on clinically-oriented basic research within the musculoskeletal system and coordinates the experimental research of the department. The interdisciplinary working group (covering molecular medicine, biology, and biochemistry) consists of 12 employees (including four PhD students). Our research focuses on the pathophysiology and therapy of cartilage diseases (e.g. cartilage trauma and osteoarthritis), the role of mesenchymal stem cells in skeletal disease and tissue regeneration as well as cell-biomaterial interactions (e.g. surface functionalization of implants and nanotechnology). Research projects are currently funded by the DFG, the BMBF and the Center for Musculoskeletal Research Ulm. In 2013, the research prize of the German Society of Arthroplasty (AE-Preis) was awarded for one of our studies on biofunctionalization of implant surfaces.



Navigation system for the implantation of orthopedic implants (e.g. total knee replacement)

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Selected Publications:

- *Neuerburg C, Recknagel S, Fiedler J, Groll J, Moeller M, Bruellhoff K, Reichel H, Ignatius A, Brenner RE (2013) Ultrathin sP(EO-stat-PO) hydrogel coatings are biocompatible and preserve functionality of surface bound growth factors in vivo. J Mater Sci Mater Med, 24: 2417-2427.*
- *Fiedler J, Ozdemir B, Bartholomä J, Plettl A, Brenner RE, Ziemann P (2013): The effect of substrate surface nanotopography on the behavior of multipotent mesenchymal stromal cells and osteoblasts. Biomaterials, 34: 8851-8859.*
- *Fraitzl CR, Kappe T, Pennekamp F, Reichel H, Billich C (2013) Femoral head-neck offset measurements in 339 subjects: Distribution an implications for femoroacetabular impingement. Knee Surg Sports Traumatol Arthrosc 21: 1212-1217.*
- *Bieger R, Ignatius A, Decking R, Claes L, Reichel H, Dürselen L (2012) Initial stability and strain distribution of cementless hip stems as a function of implant design and length. Clin Biomech (Bristol, Avon) 27:158-164.*
- *Kappe T, Kocak T, Bieger R, Reichel H, Fraitzl CR (2011) Radiographic risk factors for labral lesions in femoroacetabular impingement. Clin Orthop Rel Res 469: 3241-3247.*

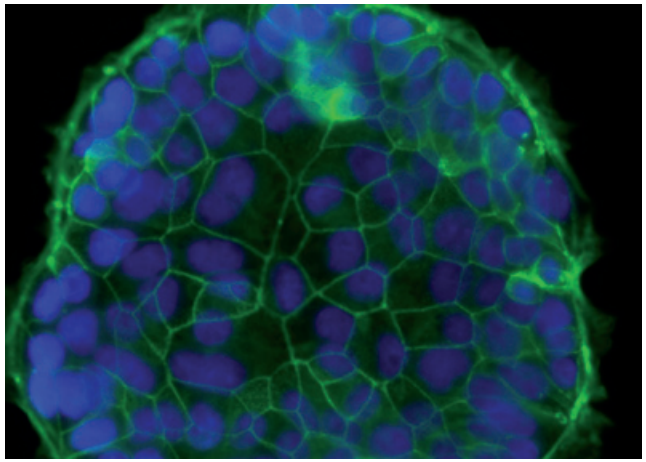


Department of Otorhinolaryngology

Head of Department: Prof. Dr. Thomas K. Hoffmann, M.D.

Keywords: Head&neck cancer | oncology | rhinology | regenerative medicine

The Department of Otorhinolaryngology (ORL), certified according to DIN EN ISO, offers state-of-the-art diagnostics and therapy in the field of oncology and reconstructive surgery, rhinology, ear surgery, including cochlear and middle ear implantation, as well as computer/robot-assisted surgery. It has been certified as a “Head and Neck Cancer Center” by the German Cancer Society and is part of the Comprehensive Cancer Center Ulm (CCCU). Our special expertise lies in the interdisciplinary treatment of head and neck cancer, including high-end surgical resection with plastic reconstructions as well as (chemo/immuno) radiation in a primary, adjuvant and palliative setting. The scientific focus and expertise of our department centers on tumor immunology and the integration of immunotherapy strategies



Fluorescence microscopy of BHY-2 cells, a human oral SCC cell line, for localization and visualization of actin filaments (f-actin: PromoFluor-488, phalloidin; cell nuclei: counterstained with DAPI)

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into standard treatment. Thus, a variety of clinical trials are offered which have been approved by the local ethical board. Our extensive expertise in rhinology is not only based on septorhinoplasty, surgical nasal reconstruction and anterior skull base surgery but also includes research activities such as intranasal air conditioning and the numerical simulation of intranasal air flow in computer models.

Furthermore, our recognized research group specializing in regenerative medicine is focused on cartilage tissue engineering for reconstructive head and neck surgery, and regeneration of salivary gland tissue using stem cells for patients suffering from severe dryness of mouth (xerostomia). The division of phoniatry and audiology has established an important partnership with the Hearing Implant Center which also performs high standard phonosurgery. The teaching of medical students and international guests is performed in a multidisciplinary skills lab and recognized operation courses.

The ORL Department at Ulm University covers an area of over two million inhabitants and is comprehensively equipped with four operating rooms, four intensive care beds and a 24 hour emergency service as well as an optimal research lab with a translational scientific focus to ensure high-end patient care.

Selected Publications:

- *Bermueller C, Schwarz S, Elsaesser AF, Sewing J, Baur N, von Bomhard A, Scheithauer M, Notbohm H, Rotter N. Marine collagen scaffolds for nasal cartilage repair: prevention of nasal septal perforations in a new orthotopic rat model using tissue engineering techniques. Tissue Eng Part A. 2013 Oct;19(19-20):2201-14.*
- *Scheithauer MO, Rotter N, Lindemann J, Schulz M, Rettinger G, Veit JA. The auricle's cavum conchae composite graft in nasal reconstruction. Am J Rhinol Allergy. 2013 Mar-Apr;27(2):e53-7. doi: 10.2500/ajra.2013.27.3883.*
- *Hoffmann TK, Schuler PJ, Bankfalvi A, Greve J, Heusgen L, Lang S, Mattheis S. Comparative analysis of resection tools suited for transoral robot-assisted surgery. Eur Arch Otorhinolaryngol. 2013 Jul 12.*
- *Lindemann J, Rettinger G, Kröger R, Sommer F. Numerical simulation of airflow patterns in nose models with differently localized septal perforations. Laryngoscope. 2013 Sep;123(9):2085-9. doi: 10.1002/lary.23653. Epub 2013 Jul 2.*
- *Schuler PJ, Harasymczuk M, Schilling B, Saze Z, Strauss L, Lang S, Johnson JT, Whiteside TL. Effects of adjuvant chemoradiotherapy on the frequency and function of regulatory T cells in patients with head and neck cancer. Clin Cancer Res. 2013 Dec 1;19(23):6585-96. doi: 10.1158/1078-0432.CCR-13-0900. Epub 2013 Oct 4.*



Sculpture of “Roberta and the Flying Horse”
by Elisabeth Wagner

Department of Pediatrics and Adolescent Medicine

Head of Department: Prof. Dr. Klaus-Michael Debatin

Keywords: Pediatrics | Hematology/Oncology | Endocrinology | Cardiology | Neonatology | Neurology | Immunology | Bone Marrow Transplantation | Intensive Care | Gastroenterology | Nephrology | Hepatology | Hemostaseology | Mucoviscidosis | Rheumatology | Apoptosis

At the Department of Pediatrics and Adolescent Medicine of Ulm University, we offer comprehensive and high-quality patient care for children and adolescents. The hospital has a capacity of 117 beds and employs over 400 personnel. It is our goal to obtain the best treatments possible based on the latest diagnostic and therapeutic concepts.

All relevant areas of expertise are represented at our hospital which has gained a high reputation, both nationally and internationally, in the areas of bone marrow and stem cell transplantation, solid tumors, leukemia and blood diseases, immunology, preterm and neonatal medicine and hormone-related diseases, such as diabetes. We are a supraregional center specialized in the fields of cardiovascular disease, gastrointestinal disease, kidney disease and mucoviscidosis.

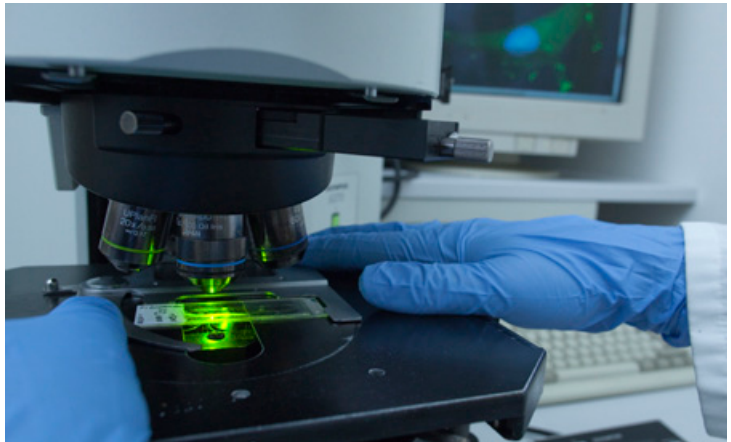
We also make provision for all the support and guidance needed during and after a stay at our hospital. In our new buildings most rooms are constructed as mother-child units in order to allow parents to stay with their child during treatment. Additional services include apartments for parents of inpatients, playrooms, visits of clown doctors, bedside learning, art and music therapy, interpreters, dietary advice, a consultation service as well as sociomedical and psychosocial aftercare.

Our research has a strong focus on hematology and oncology. It is dedicated to understanding the role of cell death (apoptosis) and cell death signaling in diseases, such as cancer, with the aim of developing new therapies from this knowledge. A particular focus is centered on strategies to overcome treatment resistance in leukemia, neuroblastoma and brain tumors.

In the area of stem cell transplantation and immunology, our work groups have significantly contributed to the development of blood stem cell and bone marrow transplantations and have characterized the genetic heirs of several forms of severe combined immune defects (SCID).

Our research team specializing in pediatric endocrinology and diabetes aims to elucidate the molecular causes of endocrine and metabolic diseases by focusing on special forms of diabetes mellitus and rare adipose tissue disorders such as lipodystrophy. Furthermore, we study the causes and effects of obesity in childhood and adolescence and develop novel therapy strategies.

Other important research fields of our department are non-malignant hematological diseases, primary care and developmental prognosis of preterm infants, as well as attention-deficit/hyperactivity disorder (ADHD). Our largest research projects are described separately in the *Research Centers* section of this report.



Immunofluorescence analysis of a glioblastoma cell.

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Selected Publications:

- *Keuper M, Wernstedt Asterholm I, Scherer PE, Westhoff MA, Möller P, Debatin KM, Strauss G, Wabitsch M, Fischer-Posovszky P (2013): TRAIL (TNF-related apoptosis-inducing ligand) regulates adipocyte metabolism by caspase-mediated cleavage of PPARgamma. Cell Death Dis 4:e474.*
- *Hartmann N, Messmann JJ, Leithäuser F, Weiswange M, Kluge M, Fricke H, Debatin KM, Strauss G (2013): Recombinant CD95-Fc (APG101) prevents graft-versus-host disease in mice without disabling antitumor cytotoxicity and T-cell functions. Blood 121:556-65.*
- *Loeder S, Schirmer M, Schoeneberger H, Cristofanon S, Leibacher J, Vanlangenakker N, Bertrand MJ, Vandenabeele P, Jeremias I, Debatin KM, Fulda S (2012): RIP1 is required for IAP inhibitor-mediated sensitization of childhood acute leukemia cells to chemotherapy-induced apoptosis. Leukemia 26:1020-9.*
- *Schulz AS, Glatting G, Hönig M, Schütz C, Gatz SA, Grewendorf S, Sparber-Sauer M, Muche R, Blumstein N, Kropshofer G, Suttorp M, Bunjes D, Debatin KM, Reske SN, Friedrich W (2011): Radioimmunotherapy-based conditioning for hematopoietic cell transplantation in children with malignant and nonmalignant diseases. Blood 117:4642-50.*
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Surgery applying the da Vinci SI HD System®.

Department of Urology

Acting Director of the Department: PD Dr. Florian Jentzmik

Keywords: Minimal invasive surgery | neobladder | prostate cancer | systemic therapy | urooncology

The Department of Urology is one of the largest urological centers in Germany that offers the whole spectrum of modern diagnostics and therapy in both adult and pediatric urology. Fifteen physicians (seven specialists and eight residents), ten surgical nurses, 56 carers and general nurses as well as eight administrative secretaries arrange an optimal daily academic and clinical routine.
Our commitment is to quality and value by providing facilities for advanced surgical procedures combined with friendly and professional care. Our department has 55 beds with all rooms offering the privacy and comfort of en-suite facilities, satellite TV and telephone. The hospital has four theaters (ORs), one minor procedures theater, a six-bed intensive care unit and a seven-bed high dependency unit. These facilities, combined with the latest technology and on-site support services, enable us to perform a wide range of procedures from routine investigations to complex surgery. This specialist expertise is supported by a caring and professional medical staff that, together with dedicated nursing teams and resident medical officers on duty 24 hours a day, provides care within a friendly and comfortable environment.

The Department of Urology is particularly specialized in the treatment of urological malignancies. It is this clinic that conceived and developed the ileum neobladder, which has today become the most accepted form of continent urinary diversion worldwide for patients with invasive bladder cancer. Moreover, the Department of Urology and its members possess the skills and expertise for the treatment of localized and metastatic prostate, renal and testicular cancer. Several of our surgeons are specifically specialized in conventional and robotic-assisted (da Vinci SI HD System®) laparoscopic radical prostatectomy. All therapeutic procedures are based on interdisciplinary tumor board decisions.



Operating at the da Vinci SI HD System®.

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As one of the first established centers we offer a novel endoscopic technique, the thulium laser transurethral enucleation (ThuLEP) for the treatment of benign prostatic hyperplasia that can even be used in patients under anticoagulant/antiplatelet therapy. As a matter of course, we also offer up-to-date reconstructive, endoscopic and female urology surgery as well as special consultation hours for andrology and pediatric urology. Moreover, we possess an ultra-modern extracorporeal shock-wave lithotripter to locate urinary stones by applying ultrasound as well as X-ray technology.

The Department of Urology at Ulm is also active in clinical (phase I-IV) trials as well as fundamental research. We have a fully equipped laboratory for experimental/molecular urology as well as molecular genetics of prostate cancer that is headed by two experienced biologists. Our main focus is on the discovery of potentially clinically-relevant alterations in tumor biology and tumor cell signaling. This research area with its clear translational background is currently being established in close collaboration with the clinic.

Selected Publications:

- *Schrader AJ, Boegemann M, Ohlmann C-H, Schnoeller TJ, Krabbe L-M, Hajili T, Jentzmik F, Stoeckle M, Schrader M, Herrmann E, Cronauer MV (2013): Enzalutamide in castration resistant prostate cancer patients progressing after docetaxel and abiraterone. Eur Urol. [Epub ahead of print].*
- *Steinestel J, Cronauer MV, Müller J, Al Ghazal A, Skowronek P, Arndt A, Kraft K, Schrader M, Schrader AJ, Steinestel K (2013): Overexpression of p16INK4a in urothelial carcinoma in situ is a marker for MAPK-mediated epithelial meschenchymal transition but is not related to human papilloma virus infection. PLoS ONE, 8(5): e65198.*
- *Zengerling F, Streicher W, Schrader AJ, Schrader M, Nitzsche B, Cronauer MV, Höpfner M (2012): Effects of sorafenib on C-terminally truncated androgen receptor variants in human prostate cancer cells. Int J Mol Sci.13(9):11530-42.*
- *Jentzmik F, Schrader AJ, de Petriconi R, Hefty R, Mueller J, Doetterl J, Eickhoff A, Schrader M (2012):The ileal neobladder in female patients with bladder cancer: long-term clinical, functional, and oncological outcome. World J Urol. 30(6):733-9.*
- *Rinckleb AE, Surowy HM, Luedeke M, Varga D, Schrader M, Hoegel J, Vogel W, Maier C (2012): The prostate cancer risk locus at 10q11 is associated with DNA repair capacity. DNA Repair. 11(8):693-701.*

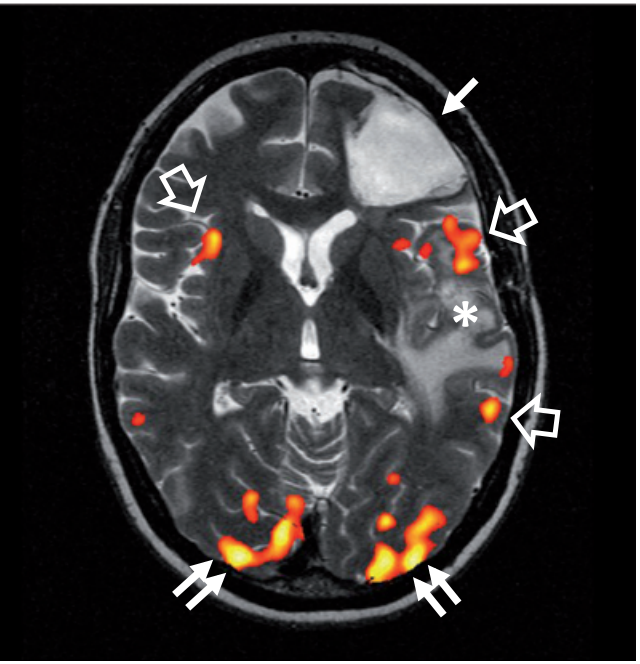


Figure 1 demonstrates a fMRI study of a patient with a relapsing malignant brain tumor (glioblastoma multiforme) of the left hemisphere (asterisk). A defect anterior to the current tumor location marks the site of the primary glioblastoma location (closed arrow). fMRI was applied to visualize the important brain area for speech recognition (Wernicke) near the site of the current tumor localization prior to a second operative resection. Active areas are highlighted by red color in fMRI (open arrow). The typical coactivation of the visual cortex is also highlighted (double arrow).

Department of Diagnostic and Interventional Radiology

Head of Department: Prof. Dr. Meinrad Beer

Keywords: Functional imaging | molecular and metabolic imaging | tissue typing | minimal-invasive interventional procedures

The department provides all radiological services for Ulm University Medical Center as a tertiary hospital center. Additionally, it supplies two further hospital centers, one focused on Neurosciences and the other serving as a secondary hospital center. The department is equipped with cutting-edge technology.

Three divisions have been established. The Division of Neuroradiology (headed by Prof. B. Schmitz) was founded some years ago and has rapidly grown to encompass the fields of both diagnostic and interventional neuroradiology. The interventional treatment of intracerebral aneurysms has been expanded to include flow diversion in addition to surgical clipping and coiling procedures. The interventional treatment of acute stroke patients has considerably been improved through the use of stent retrievers.

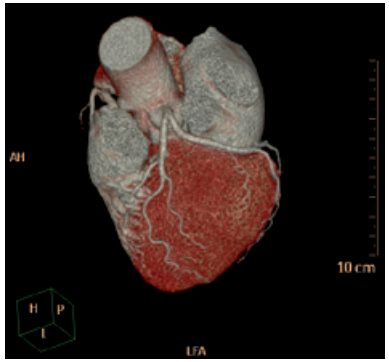
The impact of functional neuroimaging has significantly increased in recent years. The Division of Neuroradiology focuses its clinical and scientific interests especially on the areas of speech production and recognition by using functional MRI techniques (fMRI). fMRI studies allow a precise planning of primary surgery in brain tumor patients (figure 1). Additionally, fMRI studies in obese patients receiving minimal invasive therapy with a balloon catheter were started in order to analyse the interdependency between obesity and brain activation.

Two divisions were founded in 2013. The Division of Interventional Radiology performs a wide range of hepatic, vascular and biopsy interventions. The second division, the Division of Experimental Radiology founded in 2013, serves as a core facility for imaging in cooperative projects with other departments and develops its own imaging techniques.

One project deals with new T2* techniques for determination of liver iron content. Iron overload is an increasing clinical problem. New MR techniques based on multiple flip angles allow reliable measurements even at high levels of iron overload. A recent multicenter study, headed by our department, develops and applies these new state-of-the-art MRI techniques for non-invasive liver iron monitoring.

Research activities of the department also cover the field of cardiovascular radiology. CTCA (CT-coronary angiography) is applied for the planning of coronary interventions as well as minimal-invasive heart valve replacement (TAVI). The implementation of cutting-edge technologies for lowest dose-protocols allowed a significant improvement of CTCA techniques (figure 2a+b).

Further research projects are performed in collaboration with the Core Facility Imaging (headed by Prof. V. Rasche) and the Department of Nuclear Medicine (headed by Prof. A. Beer). Future research directions encompass neuroradiologic morphometric analyses (voxel-based volumetry), oncologic, metabolic and molecular imaging techniques (31P-MR-Spectroscopy and Diffusion-weighted Imaging -DWI) and, finally, noninvasive MRI-based tissue typing techniques (T1/T2/T2*-mapping and 1H-double triggered 1H-MRS).



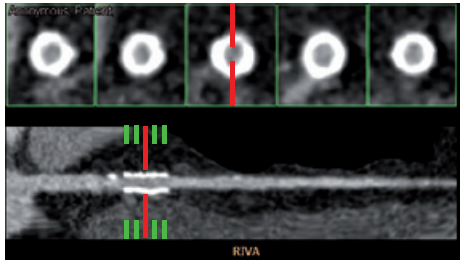


Figure 2a shows the superb 3D-visualization of the left main coronary branch with its two main side branches (LAD and CX). State-of-the-art reconstruction algorithms allow the stretched presentation of the complete course of single arteries as outlined in figure 2b. Improved CT-techniques enable the sight through coronary stents.

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Selected Publications:

- *Characteristics, changes and influence of body composition during a 4486 km transcontinental ultramarathon: results from the Transeurope Footrace mobile whole body MRI-project. Schütz UH, Billich C, König K, Würslin C, Wiedelbach H, Brambs HJ, Machann J. BMC Med. 2013;11: 122 (Impact=6.7).*
- *Liver iron content determined by MRI: spin-echo vs. gradient-echo. Juchems MS, Cario H, Schmid M, Wunderlich AP. Rofo. 2012;184: 427-31 (Impact:2.8)*
- *Diffusion-weighted MR imaging in comparison to integrated [19F]-FDG PET/CT for N-staging in patients with lung cancer. Pauls S, Schmidt SA, Juchems MS, Klass O, Luster M, Reske SN, Brambs HJ, Feuerlein S. Eur J Radiol. 2012;81: 178-82 (Impact=2.5).*
- *Substantial and reversible brain gray matter reduction but no acute brain lesions in ultramarathon runners: experience from the TransEurope-FootRace Project. Freund W, Faust S, Birklein F, Gaser C, Wunderlich AP, Müller M, Billich C, Juchems MS, Schmitz BL, Grön G, Schütz UH. BMC Med. 2012;10: 170 (Impact=6.7).*
- *Quantification of aortic valve area at 256-slice computed tomography: comparison with transesophageal echocardiography and cardiac catheterization in subjects with high-grade aortic valve stenosis prior to percutaneous valve replacement. Klass O, Walker MJ, Olszewski ME, Bahner J, Feuerlein S, Hoffmann MH, Lang A. Eur J Radiol. 2011;80: 151-7 (Impact=2.5).*



Department of Nuclear Medicine

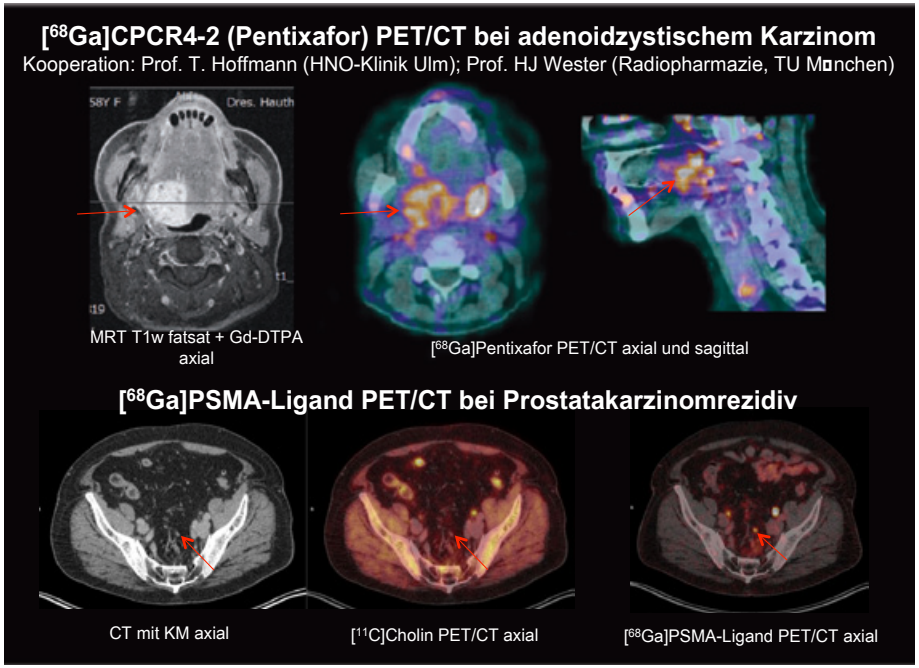
Head of Department: Prof. Dr. Ambros J. Beer (since February 2014);
Prof. Dr. Sven Norbert Reske (until February 2014)
Keywords: PET/CT | prostate cancer | pharmacokinetic modeling | thyroid cancer | molecular imaging

The Department of Nuclear Medicine provides the whole spectrum of diagnostic and therapeutic methods needed for a “tertiary referral center” setting.

The research focus of the Nuclear Medicine Clinic is the development of PET- and PET/CT- based molecular imaging techniques and targeted internal radiotherapy. The available infrastructure includes a molecular and cell biology working group, a radiochemistry section, a dosimetry and a tracer kinetic modeling group, a fully equipped PET center, including a cyclotron, radiochemistry and pharmaceutical laboratories, and one PET/CT scanner. A “small animal PET scanner” is also available at the institute.

The research focus is in the fields of tumor biology, PET and PET/CT imaging, radiotracer development, with a special emphasis on prostate cancer imaging, and the development of strategies for targeted radiotherapy with monoclonal antibodies. State-of-the-art medical physics expertise is provided in dosimetry, PET and PET/CT imaging, tracer kinetic analysis and pharmacokinetic modeling.

Current projects focus on the development of radiolabeled peptides for imaging and staging prostate cancer. Highly specific Ga-68 labeled peptides binding within the picomolar range to prostate-specific membrane antigen (PSMA) are of special interest and are already in clinical use for imaging relapsing prostate cancer. A new focus is on multimodal multiparametric imaging and analysis of tumor biology by combining morphological, functional and molecular imaging from PET and MRI.



The management of thyroid diseases, with a particular focus on cancer therapy, represents a main field of interest in patient care, as well as novel therapies with alpha-emitters such as Xofigo, for bone metastases, and targeted therapies such as PRRT (radiopeptide therapy targeted against the somatostatin receptor) in neuroendocrine malignancies.

Studies on individualized dosimetry to calculate tailored therapy activities for various radionuclides (dose escalation) have in the past resulted in optimized care for the conditioning of patients by using monoclonal antibodies in the preparation of stem cell transplantation in high-risk leukemia.

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Selected Publications:

- *Rauscher I, Eiber M, Souvatzoglou M, Schwaiger M, Beer AJ: PET/MR in Oncology: Non-18F-FDG Tracers for Routine Applications. J Nucl Med. 2014 May 12;55(Supplement 2):25S-31S.*
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- *Baur B, Andreolli E, Al-Momani E, Malik N, Machulla H-J, Reske SN.and Solbach C (2014): Synthesis and labelling of Df-DUPA-Pep with gallium-68 and zirconium-89 as new PSMA ligands, Journal of Radioanalytical and Nuclear Chemistry, DOI 10.1007/s10967-013-2876-1.*
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Staff from the department demonstrate the tools for high precision patient positioning which is essential in modern treatment techniques such as rapid arc.

Department of Radiotherapy and Radiooncology

Head of Department: Prof. Dr. Thomas Wiegel

Keywords: Chemotherapy | prostate cancer | radiotherapy | resistance | tumor risk

The department has a staff of 60 employees specialized in the fields of medicine, physics, biology, informatics, radiation technique and nursing, as well as administrative staff. The team takes care of 1,100 new patients every year. Basic and clinical research and development focus on the following topics:

Cellular Response to Cancer Treatment

With regards to the importance of combined treatment modalities involving radiotherapy, cell-biological studies on the influence of androgen supply on chemo- and radiosensitivity of prostate cancer cells are conducted. Cell survival, gene expression and functionality, DNA damage and repair are major objects of research.

Individualized Risk Assessment

The multi-institutional study PASSOS aims to assess the risk of second cancer and of heart disease after radiotherapy for breast cancer. Retrospective dosimetry is carried out in the treatment plans of women whose heart was co-exposed during breast irradiation. In close collaboration with the Department of Gynecology at Ulm and with the University Hospital in Mainz, we address the risk of heart disease depending on the individual radiation dose and other treatment-related parameters as well as general cardiovascular risk factors (e.g. age, weight). The study is funded by the Federal Ministry of Education and Research.

Improving Prostate Cancer Treatment

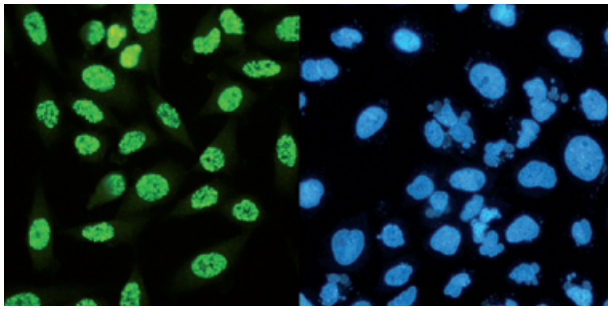
Prostate cancer is the most common cancer in adult men. When assessing different therapy options, decision-making is largely influenced by aspects affecting quality of life. To reinforce decisions based on objective criteria, detailed analyses of stage-of-disease dependent treatment outcome are mandatory. By means of our data and expertise we contribute to the periodical updates in treatment guidelines for prostate cancer.

Up-to-date Treatment at Two Sites

A most recent radiation technique known as RapidArc® is currently available on two linear accelerators in our department. In this treatment mode, the head of the therapy device moves around the longitudinal patient axis while continuously adjusting its aperture to the tumor shape which changes with the shifting angle. This strategy aims to minimize the exposure of normal tissue to radiation. Since its opening in 2011, our sister clinic in Ehingen has treated 800 patients. Similarly, as at Ulm, the panel of radiation modalities includes IMRT, RapidArc® and IORT.

Involvement in Clinical Studies:

PNET/Medulloblastoma and ependymoma in young patients: HIT-2000.
Prostate cancer: PREFERE, ART-2.
Squamous cell carcinoma of the head and neck: DÖSAK pN1.
Hodgkin's lymphoma: PVAG-14; HD 16,17,18.
Spinal cord metastasis: SCORE-2.



Radiation damage visualized in the nuclei of prostate cancer cells (left: γ-H2AX). Unless the damage is repaired, cell death will ultimately occur (right: apoptosis).

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Selected Publications:

- *Heidenreich A, Bastian PJ, Bellmunt J, Bolla M, Joniau S, van der Kwast T, Mason M, Matveev V, Wiegel T, Zattoni F, Mottet N. EAU Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent-Update 2013. Eur Urol. 2014 Jan;65(1):124-37.*
- *Heidenreich A, Bastian PJ, Bellmunt J, Bolla M, Joniau S, van der Kwast T, Mason M, Matveev V, Wiegel T, Zattoni F, Mottet N. EAU Guidelines on Prostate Cancer. Part II: Treatment of Advanced, Relapsing, and Castration-Resistant Prostate Cancer. Eur Urol. 2013 Nov 12. [Epub ahead of print]*
- *Bottke D, Golz R, Störkel S, Hinke A, Siegmann A, Hertle L, Miller K, Hinkelbein W, Wiegel T. Phase 3 Study of Adjuvant Radiotherapy Versus Wait and See in pT3 Prostate Cancer: Impact of Pathology Review on Analysis. Eur Urol. 2013 Aug;64(2):193-8.*
- *Bartkowiak D, Humble N, Suhr P, Hagg J, Mair K, Polivka B, Schneider U, Bottke D, Wiegel T. Second cancer after radiotherapy, 1981-2007. Radiother Oncol. 2012 Oct;105(1):122-6.*
- *Briganti A, Wiegel T, Joniau S, Cozzarini C, Bianchi M, Sun M, Tombal B, Haustermans K, Budiharto T, Hinkelbein W, Di Muzio N, Karakiewicz PI, Montorsi F, Van Poppel H: Early salvage radiation therapy does not compromise cancer control in patients with pT3No prostate cancer after radical prostatectomy: results of a match-controlled multi-institutional analysis. Eur Urol. 2012 Sep;62(3):472-87.*



In the Molecular Biology Lab

Department of Psychiatry and Psychotherapy I

Head of Department: Prof. Dr. Wolfgang P. Kaschka

Keywords: Affective disorders | mechanisms of antidepressant action | neurobiology | electrophysiology | suicide research

The South Württemberg Center for Psychiatry in Ravensburg provides comprehensive clinical psychiatric care services for a population of approximately 450,000 people. There are seven specialist departments (Depression, Psychosomatic and Psychotherapy, Geriatric, General-Social, Addiction, Child and Youth, and Forensic). In an average year, approximately 4,000 inpatients pass through the center. The academic staff includes 39 physicians and 21 psychologists. The percentage of female employees is 50%.

Psychiatric Services

The hospital provides specialized wards for patients with affective disorders and personality disorders. There is an outpatient clinic with special services for patients with affective disorders (burnout syndrome, lithium clinic), dementias (memory clinic) and addiction. A crisis intervention unit also provides home treatment. An integrated system of quality management is employed (KTQ).

Research Topics

Neurophysiological Research

Electrophysiological techniques are employed to characterize differences in habituation patterns between those patients identified as at particular risk of suicide and those that are not. Particular variations found in components (P300) of patient encephalograms and in electrodermal activity (EDA) taken during auditory discrimination tests are subjected to further analysis and intergroup comparison (suicide attempters vs controls). The combination of clinical observation with electrophysiological profiling is used to develop biological risk markers for suicidal behavior.

Molecular Biological Research

We use the nematode worm *Caenorhabditis elegans* as a model system. The combination of a simple body plan and sequenced genome, together with established techniques for genetics and cell/molecular biology, makes *C. elegans* ideal for such work. At the same time, many biochemical and signaling pathways are conserved between humans and *C. elegans*, making the application of research findings within a human context much easier.

Currently, we have three ongoing, interrelated projects in the lab:

1. Identification of temporal/cell-specific changes in Insulin/TGF-β signaling that trigger fat accumulation during diapause (metabolic depression of activity in response to stress).
   (Manuela Hörnle, Steve Hodgkinson)

2. Changes in nuclear hormone receptor binding activity in response to treatment with atypical antipsychotics.
   (Steve Hodgkinson)

3. Changes in the serotonin-guanylate cyclase signaling pathway in response to treatment with antidepressant drugs.
   (Isabelle Hellwig, Steve Hodgkinson)



On the Specialized Depression Ward

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Selected Publications:

- *Thorell LH, Wolfersdorf M, Straub R, Steyer J, Hodgkinson S, Kaschka WP, Jandl M: Electrodermal hyporeactivity as a trait marker for suicidal propensity in uni- and bipolar depression. Journal of Psychiatric Research, 2013; 47: 1925-1931.*
- *Anderson-Schmidt H, Adler L, Aly C, Anghelescu I-O, Bauer M, Baumgärtner J, Becker J, Bianco R, Becker T, Bitter C, Bönsch D, Buckow K, Budde M, Bührig M, Deckert J, Demiroglu SY, Dietrich D, Dümpelmann M, Engelhardt U, Fallgatter AJ, Feldhaus D, Figge C, Folkerts H, Franz M, Gade K, Gaebel W, Grabe H-J, Gruber O, Gullatz V, Gusky L, Heilbronner U, Helbig K, Hegerl U, Heinz A, Hensch T, Hiemke C, Jäger M, Jahn-Brodmann A, Juckel G, Kandulski F, Kaschka WP, Kircher T, Koller M, Konrad K, Kornhuber J, Krause M, Krug A, Lee M, Leweke M, Lieb K, Mammes M, Meyer-Lindenberg A, Mühlbacher M, Müller MJ, Nieratschker V, Nierste B, Ohle J, Pfennig A, Pieper M, Quade M, Reich-Erkelenz D, Reif A, Reitt M, Reininghaus B, Reininghaus EZ, Riemenschneider M, Rienhoff O, Roser P, Rujescu D, Schennach R, Scherk H, Schmauss M, Schneider F, Schosser A, Schott BH, Schwab SG, Schwanke J, Skrowny D, Spitzer C, Stierl S, Stöckel J, Stübner S, Thiel A, Volz H-P, von Hagen M, Walter H, Witt SH, Wobrock T, Zielasek J, Zimmermann J, Zitzelsberger A, Maier W, Falkai PG, Rietschel M, Schulze TG: The "DGPPN-Cohort": a national collaboration initiative by the German Association for Psychiatry and Psychotherapy (DGPPN) for establishing a large-scale cohort of psychiatric patients. Eur Arch Psychiatry Clin Neurosci, 2013; 263:695-701. Article first published online: 03 April 2013, DOI 10.1007/s00406-013-0401-8.*
- *Jandl, M, Steyer, J, Kaschka, WP: Adolescent attention deficit hyperactivity disorder and susceptibility to psychosis in adulthood: a review of the literature and phenomenological case report. Early Intervention in Psychiatry, 2012; 6(1): 11-20. Article first published online: 6 SEP 2011, DOI: 10.1111/j.1751-7893.2011.00293.X.*
- *Kaschka, WP, Korczak, D, Broich, K: Modediagnose Burnout. Dtsch Ärztebl Int, 2011; 108 (46): 781-787.*
- *Hodgkinson, S, Kaschka, WP: Patterns of hydrophobicity found in the first and second trans-membrane domains of solute transporters suggest a possible role in nascent protein anchoring and organization. J Bioinform Comput Biol, 2011; 9 (4): 471-488 (DOI No.: 10.1142/S0219720011005367).*



Department of Psychiatry and Psychotherapy II

Head of Department: Prof. Dr. Thomas Becker

Keywords: Mental health services research | process outcome | health economics | meta-analyses | gender-specific aspects | dementia | schizophrenic psychoses | stigma

The Clinic of Psychiatry and Psychotherapy II at *Bezirkskrankenhaus Günzburg* offers mental health care consisting of inpatient services, two day care units, an outpatient clinic and home treatment for 671,000 inhabitants of a catchment area in rural Bavaria.
The department has two research groups: *Psychoimmunology* (Prof. Dr. Karl Bechter); *Psychopathology and Psychopharmacology* (Prof. Dr. Markus Jäger); and four sections: *Health Economics and Health Services Research* (Prof. Dr. Reinhold Kilian); *Process-Outcome Research* (PD Dr. Bernd Puschner); *Geriatric Psychiatry* (Prof. Dr. Matthias Riepe); and, since 2013, *Public Mental Health* (Prof. Dr. Nicolas Rüsch).

Some of the department's numerous research projects are highlighted in the following list:

- *Clinical decision making and outcome in routine care for people with severe mental illness (CEDAR)*. To investigate the effect of clinical decision-making on crucial dimensions of clinical outcome (symptom level, quality of life, needs) by means of a multinational prospective study (funded by the European Commission, grant no. 223290).
- *Cochrane review of implementation of treatment guidelines for specialist mental health care.* The aim of this systematic review is to summarize the evidence pertaining to the effects of guideline implementation in specialist mental health care in view of specific implementation strategies (funded by BMBF, ref. code/FKZ 01KG1109).



Bezirkskrankenhaus Günzburg
with the Department of Psychiatry
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- *Effectiveness and cost-efficiency of contracts in integrative care from patients suffering serious mental illnesses in real surroundings with particular attention to improvement of empowerment and quality of life (IVPOWER)*. The focus of this project is the transregional analysis of effectiveness and cost-effectiveness of contracts for integrated care programs according to NWpG (NetzWerk psychische Gesundheit)) compared to the usual treatment in real surroundings (funded by BMG, ref. code/FKZ II A 5 – 2513 FSB 012).
- *Psychiatric discourse on desire for children and parenthood among people with mental illnesses.* The study investigates the psychiatric discourse as well as subjective attitudes of mental health professionals in regard to desire for children and parenthood (study in collaboration with the Institute of the History, Philosophy and Ethics of Medicine, Ulm University; funded by DFG, ref. code/GZ KR 3879/1-1).
- *Identification of psychopathological course types in schizophrenic psychoses.* To identify homogenous subgroups of schizophrenic disorders with respect to the psychopathological course and outcome and to correlate these subtypes with neurobiological markers (funded by DFG, ref. code/GZ JA 1742/2-1).
- *Efficacy and safety of add-on therapy with calcium-antagonist nilvadipine in patients with mild to moderate Alzheimer's disease (NILVAD)*. The study tests the efficacy and safety of nilvadipine in 500 subjects with mild to moderate AD over a treatment period of 18 months (funded by the European Commission, grant no. 297093).

Selected Publications:

- *Koesters M, Guaiana G, Cipriani A, Becker T, Barbui C (2013): Agomelatine efficacy and acceptability revisited: systematic review and meta-analysis of published and unpublished randomised trials. Br J Psychiatr, 203:179-187.*
- *Puschner B, Neumann P, Jordan H, Slade M, Fiorillo A, Giacco D, Égerházi A, Ivánka T, Bording MK, Sørensen HØ, Bär A, Kawohl W, Loos S (2013): Development and psychometric properties of a five-language multiperspective instrument to assess clinical decision making style in the treatment of people with severe mental illness (CDMS). BMC Psychiatr 13:1-10.*
- *Kilian R, Steinert T, Schepp W, Weiser P, Jaeger S, Pfiffner C, Frasch K, Eschweiler GW, Messer T, Croissant D, Becker T, Längle G (2012): Effectiveness of antipsychotic maintenance therapy with quetiapine in comparison with risperidone and olanzapine in routine schizophrenia treatment: results of a prospective observational trial. Eur Arch Psychiatry Clin Neurosci 262:589-598.*
- *Neumeister K, Riepe MW (2012). Synergistic effects of antidementia drugs on spatial learning and recall in the APP23 transgenic mouse model of Alzheimers disease. Int J Alzheimer's Dis 30:245-251.*
- *Jäger M, Haack S, Becker T, Frasch K (2011): Schizoaffective disorder – an ongoing challenge for psychiatric nosology. Eur Psychiatr 26(3), 159-165.*



Transcranial direct current stimulation (tDCS). Two large sponge electrodes are placed on the subject's skull to apply a small electric current (1 – 2 mA) for 10 – 30 min. This current polarizes cortical neural networks, resulting in either facilitation of network function (anode) or in gradual inhibition (cathode). The bi-frontal montage demonstrated in the picture has been established as stimulation site with therapeutic potency in the treatment of patients suffering from major depression.

Department of Psychiatry and Psychotherapy III

Head of Department: Prof. Dr. med. Dr. phil. Manfred Spitzer

Keywords: Cognitive neuroscience | event-related potentials | functional imaging | transcranial magnetic stimulation | translational research in education

The Department of Psychiatry and Psychotherapy III employs 23 physicians (13 female), 11 clinical psychologists (10 female), and 13 non-medical scientists (six female). The department combines outpatient and inpatient state-of-the-art care for patients with psychiatric disorders (three wards with 69 beds, a day hospital and outpatient clinic). A special focus is placed on psychiatric acute care since the department is responsible for mental health emergencies in the city of Ulm and surrounding districts, covering a population of approximately 220,000 people. An Institute for Behavioral Therapy on a postgraduate level was founded in 2013 and has been integrated into the department.

The department's scientific focus is on systems neuroscience aspects of mental disorders. Cognitive and affective neuroscience methods are used to understand high-level cognitive functions in normal subjects, and the development and maintenance of psychiatric disorders. Most of the research takes place in three cooperating divisions. Research on the transfer of neuroscience findings into educational practice is conducted at a dedicated research center that is part of our department and known as the Transfer Center for Neuroscience and Learning.

The division for Functional Imaging and Neuropsychology (Prof. Dr. phil. Georg Grön) includes a high-field magnetic resonance scanner dedicated to research. Brain imaging under different functional challenges is used to investigate and explore human brain functions under circumscribed experimental conditions. The focus is on mental functions (e.g. memory, reward processing, motivational and emotional processes) and dysfunctions that correlate with psychiatric disorders.



A subject is being prepared for an experimental session in the section's research-dedicated high-field magnetic resonance (MR) scanner operating at the field strength of 3.0 Tesla. He is already wearing an MR-compatible headset for communication and auditive stimulation, as well as MR-compatible video goggles over his eyes to present high resolution visual stimuli. The assistant is holding the upper part of a transmit-receive coil which will be mounted above the subject's head.

Later, after the subject has been placed in the MR-tunnel (behind the subject's head), a task will be presented through the goggles and headset. The task is the cognitive challenge during which functional magnetic resonance images are acquired at high spatial resolution.

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Employing appropriate study designs, commonalities and differences between normal and impaired brain functioning are investigated. In 2014 the actual scanner will be replaced by a new state-of-the-art high-field magnetic resonance scanner which is planned to serve as a campus-wide core-facility for all research groups working in the field of imaging neuroscience in humans.

In the division for Cognitive Electrophysiology (Prof. Dr. phil. Markus Kiefer), the scientific focus is on language, higher conceptual representation and attention. A state-of-the art 64-channel electroencephalographic recording system permits the study of brain electrical activity at high temporal resolution.

In the division for Neurostimulation (Prof. Dr. med. Thomas Kammer), the physiological background of non-invasive brain stimulation techniques, such as transcranial magnetic stimulation or transcranial DC-stimulation is explored. In clinical trials, the therapeutic potency of stimulation techniques in several psychiatric disorders is investigated.

In the Transfer Center for Neuroscience and Learning (ZNL), a multidisciplinary team of teachers, psychologists and educational scientists integrates recent neuroscience findings into practical applications in the field of education in children and adults. The general aim is to use the well-established medical model of translational research in the field of education.

Selected Publications:

- *Fladung AK, Schulze UM, Schöll F, Bauer K, Grön G (2013): Role of the ventral striatum in developing anorexia nervosa Transl Psychiatry, 3:e315.*
- *Ulrich M, Hoenig K, Grön G, Kiefer M (2013): Brain activation during masked and unmasked semantic priming: commonalities and differences. J Cogn Neurosci, 25: 2216-29.*
- *Abler B, Grön G, Hartmann A, Metzger C, Walter M (2012): Modulation of frontostriatal interaction aligns with reduced primary reward processing under serotonergic drugs. J Neurosci, 32:1329-35.*
- *Cárdenas-Morales L, Grön G, Kammer T (2011): Exploring the after-effects of theta burst magnetic stimulation on the human motor cortex: a functional imaging study. Hum Brain Mapp, 32:1948-60.*
- *Graf H, Abler B, Freudenmann R, Beschoner P, Schaeffeler E, Spitzer M, Schwab M, Grön G (2011): Neural correlates of error monitoring modulated by atomoxetine in healthy volunteers. Biol Psychiatry, 69:890-7.*



Department of Child and Adolescent Psychiatry and Psychotherapy

Head of Department: Prof. Dr. Jörg M. Fegert
Keywords: Childhood trauma | specialized outpatient clinics | psychotherapy research | clinical studies | child abuse and neglect

The department provides inpatient and outpatient care as well as day treatment for children and adolescents with psychiatric disorders and psychosocial problems: two wards for adolescents with a total of 19 beds; one ward for children with 12 beds; and a day care unit for 18 patients. The department also offers several specialized outpatient clinics: a unit for children in out of home placement, be it in foster care or institutions; a trauma unit; a tic and Tourette's unit; and, since recently, a Phelan-McDermid outpatient clinic. Additionally, a section for psychotherapy research combined with a training institute in child and adolescent behavior therapy (AZVT) and an outpatient psychotherapy clinic were established in 2009.

With an interdisciplinary team of expert researchers integrated into central research management and a competent consulting methodology, we are active in four research areas: biological and clinical research; prevention, social psychiatry and health care research; ethics, law, forensics; and family, time politics and e-Learning. All four areas have been expanded in recent years and all were very successful in raising external funding.

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We mainly focus on questions of childhood trauma, especially child (sexual) abuse, and specialize in web-based strategies of intervention and dissemination (e.g. missbrauch.elearning-kinderschutz.de, fruehehilfen-bw.de). With its aim to raise awareness of (sexual) child abuse and neglect within the medical field, the Competence Center Child Abuse and Neglect (www.comcan.de) was founded 2013 in Ulm in cooperation with the university hospitals in Heidelberg and Freiburg, and is sponsored by the Baden-Württemberg Ministry of Science, Research and the Arts (MWK). Another area of expertise involves research into non-suicidal self-injury and suicidality in adolescence by incorporating research projects on prevention, intervention and neurobiology.



Selected Publications:

- *Rassenhofer M, Spröber N, Schneider T & Fegert JM 2013, "Listening to victims: Use of a Critical Incident Reporting System to enable adult victims of childhood sexual abuse to participate in a political reappraisal process in Germany", Child Abuse & Neglect, vol. Vol 37, no. 9, pp. 654-663.*
- *Plener PL, Fischer CJ, In-Albon T, Rollett B, Nixon M.K, Groschwitz RC & Schmid M 2013, "Adolescent non-suicidal self-injury (NSSI) in German-speaking countries: comparing prevalence rates from three community samples", Social Psychiatry and Psychiatric Epidemiology, vol. 48, no. 9, pp. 1439-1445.*
- *Udvardi PT, Föhr KJ, Henes C, Liebau S, Dreyhaupt J, Boeckers TM &Ludolph AG 2013, "Atomoxetine affects transcription/ translation of the NMDA receptor and the norepinephrine transporter in the rat brain - an in vivo study", Drug Design, Development and Therapy, vol. 4, no.7, pp. 1433-46.*
- *Besier T, Pillhofer M, Botzenhart S, Ziegenhain U, Kindler H, Spangler G, Bovenschen I, Gabler S & Künster AK 2012, „Kindesmisshandlung und –vernachlässigung: Risikoscreening in der Geburtshilfe", Geburtshilfe und Frauenheilkunde, vol. 72, no. 5, pp. 397-402.*
- *Dieluweit U, Debatin K, Grabow D, Kaatsch P, Peter R, Seitz DCM & Goldbeck L 2011, "Educational and vocational achievement among long-term survivors of adolescent cancer in Germany", Pediatric Blood & Cancer, vol. 56, no. 3, pp. 432-438.*



Department of Psychosomatic Medicine and Psychotherapy

Department of Psychosomatic Medicine and Psychotherapy

Head of Department: Prof. Dr. Harald Gündel
Keywords: Emotion regulation | molecular psychosomatics | workplace mental health | trauma | psychotherapy | pain | psycho-oncology

The department offers a combined psychosomatic-psychotherapeutic inpatient and day hospital treatment. Moreover, it provides an outpatient service and psychosomatic consultation as well as liaison, which includes a psycho-oncology service. All kinds of mental disorders that can be reliably managed by means of psychotherapeutic procedures are the focus of the clinic, such as somatoform, pain, personality, eating and somatopsychic disorders, i.e., depressive or anxiety disorders in chronically ill or oncological patients. Within five different settings providing evidence-based treatments, such as group psychotherapy and relaxation training, our acute patients are provided with the best available multimodal psychotherapeutic care of an integrative university clinic. Services for “psychosomatic consultation at the workplace” have also been implemented. Medical and psychological education for students, as well as advanced education for all professions involved in psychosomatic medicine, have been structurally organized. Training institutes of psychoanalytic and psychodynamic (UPPI) and behavioral psychotherapy (AWIP) also work in association with our clinic.

Areas of research

I) Experimental research

Emotion regulation focuses on: (a) continuous emotion recognition based on psychobiological signals for utilization in cognitive-technical systems; (b) the development of computer-based emotion recognition methods using facial expressions; and (c) the advancement of an automated pain recognition system on the basis of facial expressions and psychobiological parameters.

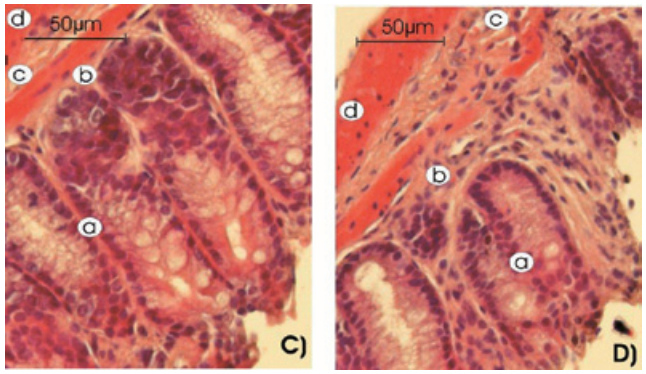
The main research aims of the Laboratory of Molecular Psychosomatics are to extend current knowledge of the mechanisms underlying: 1a) psychosocial stressor/trauma-induced development of somatic and affective pathologies; and 1b) individual differences in stress/trauma resilience; and 2) to use this mechanistic knowledge for the development of novel strategies to prevent psychosocial stress/trauma-induced pathologies. For this purpose, we employ several clinically relevant rodent models of chronic psychosocial stress/trauma and study in detail their effects on

behavioral, physiological, neuroendocrine, and immunological parameters, thereby considering individual differences in the stress-coping strategy. Our main paradigm in this context is the chronic subordinate colony housing (CSC) paradigm, which induces chronic psychosocial stress/trauma by prolonged (19 days) social subordination of male experimental mice to a larger dominant male and results, along with what is known from humans, in increased anxiety-related behavior, social deficits, enhanced alcohol consumption, pronounced changes in hypothalamus-pituitary-adrenal (HPA) axis activity/reactivity, signs of hepatic oxidative stress and inflammation, development of spontaneous colitis, and an increased risk of inflammation-related colon carcinogenesis. Interestingly, CSC mice further show basal evening hypocorticism and a reduced glucocorticoid sensitivity of peripheral target cells. The latter is of particular interest as a decreased glucocorticoid signaling following chronic psychosocial stressor/trauma exposure is also discussed in humans as a possible mediator of stress/trauma-induced pathology. Interactions between psychosocial stress, trauma, attachment and bodily reactions are studied in humans (neuroendocrinological, fMRI).

II) Health services research/Workplace mental health

In the context of workplace mental health new preventive interventions have been developed and are in the process of being evaluated. Also establishing and evaluating psychosocial counseling within the workplace setting is an important research focus. Further studies are related to work and family-issues.

Health care studies are related to an improvement of psychotherapeutic services in a prototypical region. The specific effects of inpatient and day patient treatment for patients with depression as well as the effect of psychotherapy in treating anorexia nervosa are assessed in multicenter studies.



19 days of chronic subordinate colony housing induce development of spontaneous colitis. This is indicated by an increase in the histological damage and leukocyte infiltration, depicted in two representative colonic H&E sections [a: Lamina mucosa; b: Lamina muscularis mucosae; c: Lamina submucosa; d: Lamina muscularis (circular and longitudinal mussle)] from non-stressed control mice (Fig. C; normal colon histology) and from CSC mice (Fig. D; goblet cell loss and crypt loss in locally restricted areas; infiltration reaching the Lamina muscularis mucosae; thickening of submucosal areas) (adapted from Reber et al., 2007, Endocrinology)

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Selected Publications:

- *Jongen, S, Axmacher, N, Kremers, N.A.W, Hoffmann, H, Limbrecht-Ecklundt, K, Traue, H.C. Kessler, H. (2014) An investigation of facial emotion recognition impairments in alexithymia and its neural correlates. Behavioural Brain Research. 271: 129–139*
- *Füchsl A.M, Neumann I.D, Reber S.O. (2014). Stress resilience: a low-anxiety genotype protects male mice from the consequences of chronic psychosocial stress. Endocrinology. 155(1): 117-26.*
- *Zipfel S, Wild B, Groß G, Friederich HC, Teufel M, Schellberg D, Giel KE, de Zwaan M, Dinkel A, Herpertz S, Burgmer M, Löwe B, Tagay S, von Wietersheim J, Zeeck A, Schade-Brittinger C, Schauenburg H, Herzog W, ANTOP study group, Schmidt U, Deter HC, Schneider S, Faldum A. (2014). Focal psychodynamic therapy, cognitive behaviour therapy, and optimised treatment as usual in outpatients with anorexia nervosa (ANTOP study): randomised controlled trial. Lancet. 383(9912): 127-37.*
- *Rothermund, E, Kilian, R, Hoelzer, M, Mayer, D, Mauss, D, Krueger, M, Rieger M, Guendel, H. (2012). "Psychosomatic consultation at the workplace" – a new model of care at the interface of company-supported mental health care and consultation-liaison psychosomatics: design of a mixed methods implementation study. BMC public health. 12(1): 780.*
- *Noll-Hussong M, Otti A, Wohlschlaeger A.M, Zimmer C, Henningsen P, Lahmann C, Ronel J, Subic-Wrana C, Lane R.D, Decety J, Guendel H. (2013). Neural correlates of deficits in pain-related affective meaning construction in patients with chronic pain disorder. Psychosom Med. 75(2): 124-36.*



Department of Forensic Psychiatry and Psychotherapy at the District Hospital Günzburg, Ulm University

Head of Department: Prof. Dr. Manuela Dudeck
Keywords: Forensic psychiatry | German Penal Code | prediction assessment | reasoning and rehabilitation | DBT-F

The establishment of a new Department of Forensic Psychiatry and Psychotherapy at the District Hospital Günzburg was inaugurated in November 2013 and accompanied by the founding of a new chair of forensic psychiatry and psychotherapy at the Medical University of Ulm in May 2013. The department consists of 96 places within four maximum security wards for hospital treatment, 20 places within an open plan psychiatric care unit, and an outpatient unit for the follow-up care and treatment of 60 patients at present. Besides the nursing staff and co-therapists, about 15 physicians and psychologists administer assignments related to clinical treatment, research and teaching.

The main clinical assignment consists of both guarding and treating criminal offenders with psychiatric disorders, that is, mainly substance-related and addictive disorders, schizophrenia, personality disorders, neurodevelopmental disorders and paraphilia. The patients are not admitted to the hospital by physicians

but by an appropriate court in accordance with either s.63 or s.64 of the German Penal Code or in those cases where the following requirements are fulfilled. For example, persons are not responsible for criminal conduct if, at the time of such conduct and as a result of a mental disease or defect, they lacked substantial capacity either to appreciate the criminality (wrongfulness) of their conduct or were incapable of conforming their conduct to the requirements of the law. Furthermore, there must exist an increased risk of committing further criminal acts as a result of the psychiatric disorder in question. Treatment includes both psychopharmacologic and psychotherapeutic approaches depending on the disorder itself. Also, both individual and group therapies take place. Depending on the treatment progress, the patients may be transferred to the open ward and eventually undergo outpatient forms of treatment. For this to happen, thoroughly assessed predictions and expert opinions are required. Furthermore, assignments for expert opinions regarding both criminal and social law commissioned by the courts and other prosecution departments are accepted and conducted.

The above-mentioned new chair and professorship of forensic psychiatry and psychotherapy has recently been established at Ulm University with the aim of encouraging and inspiring students of medicine, psychology and law to undertake research into forensic issues. Both basic and applied research are a key focus of interest which includes behavioral and neurobiological investigations into the regulation of emotion processes, forms of attachment as well as addictive behavior in forensic patients. This also includes psychotraumatology issues within the context of forensic psychiatry, the impact of gender on the nature and cruelty of criminal acts resulting from mental disorders, as well as the research on levels of mental health, living conditions, and human rights under imprisonment. The treatment is both offense- and disorder-oriented and bears in mind the association between the crime committed and the linked mental disorder. We intend to evaluate the application of cognitive-behavioral strategies, such as dialectic-behavioral-based psychotherapeutic approaches within the context of forensics (DBT-F), and a reasoning and rehabilitation (R&R) program in order to help in the publishing of structured, transparent and applicable treatment manuals with the aim of improving not only the treatment but also the process of prediction assessment.



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Selected Publications:

- *Arens EA, Stopsack M, Spitzer C, Appel K, Dudeck M, Völzke H, Grabe HJ, Barnow S (2013): Borderline Personality Disorder in Four Different Age Groups: A Cross-Sectional Study of Community Residents in Germany. J Pers Disord, 27(2): 196-207.*
- *Dudeck M, Drenkhahn K, Spitzer C, Barnow S, Freyberger HJ, Grabe HJ (2012): Is there an Association Between Intra-Familiar Sexual Abuse and Sexual Offences in Later Life? PsychPrax, 39(5): 217-221.*
- *Dudeck M, Drenkhahn K, Spitzer C, Barnow S, Kopp D, Freyberger HJ, Dünkel F (2011): Traumatisation and mental distress in long-term prisoners in Europe. Punishment & Society, 13(4): 403-423.*
- *Vasic N, Plichta MM, Wolf RC, Fallgatter AJ, Sosic-Vasic Z, Grön G (2012): Reduced neural error signalling in left inferior prefrontal cortex in young adults with ADHD. J. of Attention Dis., 1087054712446172.*
- *Wolf RC, Thomann PA, Sambataro F, Vasic N, Schmid M, Wolf ND (2012): Orbitofrontal cortex and impulsivity in borderline personality disorder: an MRI study of baseline brain perfusion. Eur Arch Psychiatry Clin Neurosci., 262(8): 677-685.*



Students during pre-clinical training of resin composite restorations in the new and fully equipped state-of-the art dental simulation clinic.

Department of Conservative Dentistry and Periodontology

Head of Department: Prof. Dr. Bernd Haller

Keywords: Endodontics | esthetic dentistry | minimal invasion | periodontology | restorative dentistry

The Department of Conservative Dentistry and Periodontology encompasses the disciplines of preventive and operative dentistry, endodontics, periodontology and pediatric dentistry. Our global mission is to preserve natural teeth. In restorative treatment, we are specialized in bonded tooth-colored restorations using resin composites and ceramics with the main emphasis on esthetics and minimal invasive procedures. Clinical care in endodontics covers vital pulp therapies, root canal (re-)treatments, internal bleaching and endodontic emergencies using endo microscopes and endo motors for preparation of curved root canal with NiTi rotary instruments. Patient care in periodontology covers treatment of chronic and aggressive periodontitis by scaling/root planning, surgical procedures and full-mouth disinfection. Advanced microbiological diagnostics is provided by our laboratory of oral microbiology.

Research activities are focused on in vitro and clinical testing of adhesive restorative biomaterials and on microbiological aspects of restorative, endodontic and periodontal treatment.

Team (full-time equivalency):
11 academic staff; 10.5 dental assistants; 4.5 dental/medical technicians; 2.25 administrative staff.

Dental treatment units:
15 (eight resident clinics, seven student clinics).

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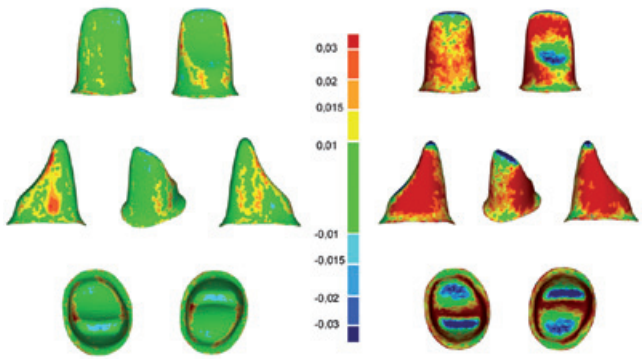
Selected Publications:

- *Haller B (2013): Which self-etch bonding systems are suitable for which clinical indications? Quintessence Int, 44(9): 645-661.*
- *Rathke A, Ostermeier V, Muche R, Haller B (2013): Reconsidering the double etching of enamel: do self-etching primers contaminate phosphoric acid-etched enamel? J. Adhes. Dent, 15(2): 107-114.*
- *Rathke A, Balz U, Muche R, Haller B (2012): Effects of self-curing activator and curing protocol on the bond strength of composite core buildups. J. Adhes. Dent, 14(1): 39-46.*
- *Rathke A, Hokenmaier G, Muche R, Haller B (2012): Effectiveness of the bond established between ceramic inlays and dentin using different luting protocols. J. Adhes. Dent, 14(2): 147-154.*
- *Tamburstuen MV, Reseland JE, Spahr A, Brookes SJ, Kvalheim G, Slaby I, Snead ML, Lyngstadaas SP (2011): Ameloblastin expression and putative autoregulation in mesenchymal cells suggest a role in early bone formation and repair. Bone, 48(2): 406-413.*



3D-analysis of different digitizing systems for dental CAD/CAM (computer-aided design/ computer-aided manufacturing) systems.

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Department of Prosthetic Dentistry

Head of Department: Prof. Dr. Ralph Luthardt

Keywords: Applied material sciences | clinical trials | computer-aided dentistry and implantology | 3D-simulation

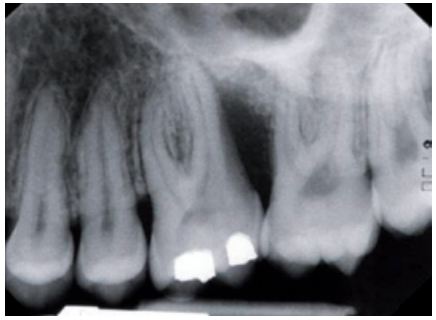
The Department of Prosthetic Dentistry administers comprehensive patient-oriented treatment after tooth loss. The primary goal is to preserve the remaining teeth and restore a healthy masticatory system. Our mission is to guarantee innovative and state-of-the-art care through the continuous ongoing education of the entire team. A total of 41 employees (66% female) are in charge of patient treatment, education and research: 13 dentists; 12 dental assistants; three trainees; five technicians; two technical assistants; six research assistants; and three external researchers. Nineteen internal and external PhD students are also being supervised. In 2012-14 the DFG Junior Academy (Nachwuchsakademie) “Dentistry” was successfully conducted.
Computer-aided manufacturing of dental restorations, 3D-planning based on cone beam CT for optimal implant positioning, minimal invasive implant surgery in addition to our synoptic patient centered treatment concept are the most innovative in prosthodontic care.

Our research topics are:

- clinical trials in oral soft-tissue management, dental implants and treatment strategies, removal of dental restorations by laser
- cross-linking clinical trials, in vitro and computer simulations (SimTOM, www.simtom.eu)
- dental material testing of advanced ceramic implants, restorations and veneering
- 3D analysis of digital workflows (from conventional and digital impressions to computer-aided manufactured restorations).

Selected Publications:

- *Rudolph H, Quaas S, Haim M, Preißler J, Walter MH, Koch R, Luthardt RG (2013): Randomized controlled clinical trial on the three-dimensional accuracy of fast-set impression materials. Clin Oral Investig, 17(5):1397-406. doi: 10.1007/s00784-012-0823-0. Epub 2012 Aug 31.*
- *Kuhn K, Rudolph H, Luthardt RG, Stock K, Diebolder R, Hibst R (2013): Er:YAG laser activation of sodium hypochlorite for root canal soft tissue dissolution. Lasers Surg Med, 45(5):339-44. doi: 10.1002/lsm.22143. Epub 2013 Jun 4.*
- *Reissmann DR, Heydecke G, Schierz O, Marré B, Wolfart S, Strub JR, Stark H, Pospiech P, Mundt T, Hannak W, Hartmann S, Wöstmann B, Luthardt RG, Böning KW, Kern M, Walter MH (2014): The randomized shortened dental arch study: temporomandibular disorder pain. Clin Oral Investig, [Epub ahead of print]*
- *Sterzenbach G, Tunjan R, Rosentritt M, Naumann M (2014): Increased tooth mobility because of loss of alveolar bone support: a hazard for zirconia two-unit cantilever resin-bonded FDPs in vitro? J Biomed Mater Res B Appl Biomater, 102(2):244-9. doi: 10.1002/jbm.b.33001. Epub 2013 Aug 30.*
- *Rudolph H, Röhl A, Walter MH, Luthardt RG, Quaas S (2014): Performance of fast-set impression materials in the reproduction of subgingival tooth surfaces without soft-tissue retraction. Int J Prosthodont, 27(4):366-75. doi: 10.11607/ijp.3752.*



Extensive bone destruction in a maxillary molar (x-ray).



The same tooth after partial periodontal regeneration and new ossification after treatment with enamel matrix proteins

Department of Oral and Maxillofacial Surgery

Acting Director of the Department: Dr. Dr. Guido Guenter Schloemer

Keywords: Cleftpalate

The Department of Maxillofacial Surgery within the Department of Odontology of Ulm University is a polyclinic equipped to provide maximum care. The work is undertaken by maxillofacial surgeons as well oral surgeons who are still in part-time education. One of these oral surgeons is female. The Institute of Radiology, furnished with all the X-ray devices relevant for this specialty, has been integrated into the department. In particular, a new digital volume tomography was supplied in 2009.

As part of the dental curriculum, the following events are held:
1. Course operation I and II.
2. Main lecture in oral maxillofacial surgery.
3. Lecture in dental medical science.
4. Lecture and course in radiology.

As part of a common research project within the departments of dentistry, the department takes part in oral maxillofacial surgery especially in the field of peri-implantitis.

With regards to maximum care, the whole spectrum of oral maxillofacial surgery as well as oral surgery is provided.

The main focus is on the treatment of patients with cleft lip and palate performed in collaboration with the departments of Otorhinolaryngology, Phoniatrics and Pediatric Audiology, Gynecology, Dermatology, and Pediatrics. Another main focus lies in the application of dental implants by employing all methods of augmentation.

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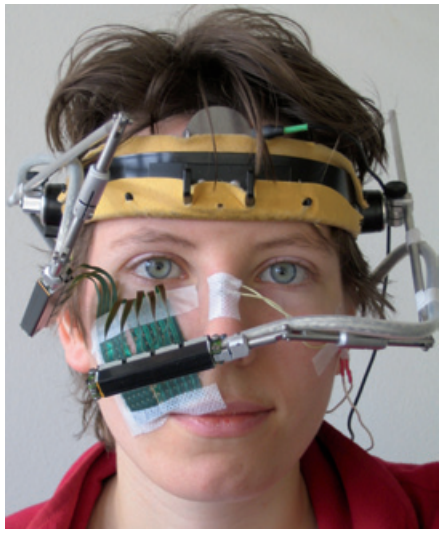
Selected Publications:

- *Sailer BF, Geibel M-A (2013): Comparative Analysis of Intraoral Radiographs with Variation of Tube Angulationto detect Insuffizient Crown Margins. International Journal of Computerized Dentistry; 16,201-2007.*
- *Schilling R, Geibel M-A (2013): Assessment of the effective Doses rom two dental cone beam Ct devices. Dentomaxillofacial Radiology;42(5):20120273.*
- *Bracher AK, Hofmann CP, Bornstedt A, Ulrici J, Geibel M-A, Hell E, Janke F, Haller B, Rasche V (2013): Ultrashort Echo Time (UTE) MR Imaging for the Assessment of Caries Lesions. Dentomaxillofacial Radiology 2013;42(6):20120321.*
- *Reiter R, Haase S, Brosch S(2012): Orofaziale Spaltbildungen; Laryngorhinootologie; 91:84-95.*
- *Reiter R, Brosch S, Lüdeke M, Fischbein E, Haase S, Pickhard A, Assum G, Schwandt A, Vogel W, Högel J, Maier Ch (2012): Genetic and environmental risk factors for submucous cleft palate European Journal of Oral Sciences; 120: 97-103.*



Surface electromyography in the face using multi-electrode arrays. This method allows the determination of basic anatomic and neurophysiologic parameters (e.g. muscle fiber directions and motor endplate locations) on the level of the smallest functional unit of human musculature, i.e. the single motor unit. Such information is of fundamental interest and is useful for optimizing functional diagnosis and therapeutic strategies.

Department of Dentofacial Orthopedics and Orthodontics

Head of Department: Prof. Dr. Dr. Bernd Lapatki
Keywords: Biomechanics | facial muscles | malocclusion | tooth movement | smart bracket

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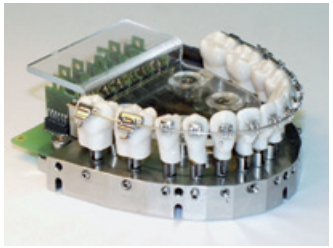
The department is an integral part of the Center of Dentistry and has approximately 25 employees that include orthodontists, postgraduate students, and scientists. The duties of the department are research, the education of dental students and specialists in orthodontics, and patient care.

Its main scientific topics lie in the fields of orthodontic biomechanics and neurophysiology of the orofacial and masticatory system. A scientific highlight is the development of smart brackets with an integrated sensor system for 3D force-moment measurements during orthodontic therapy. Quantitative knowledge of the 3D force-moment systems applied for therapeutic tooth movement is of utmost importance with regard to the predictability of tooth movement and the reduction of traumatic side-effects such as dental root resorption. Telemetric components for data and energy transmission are currently being integrated into the smart brackets to enable their future clinical application. We have also been able to realize a smart dentition which is currently applied in vitro for investigating force-moment systems exerted on the individual teeth during simulated treatment situations.

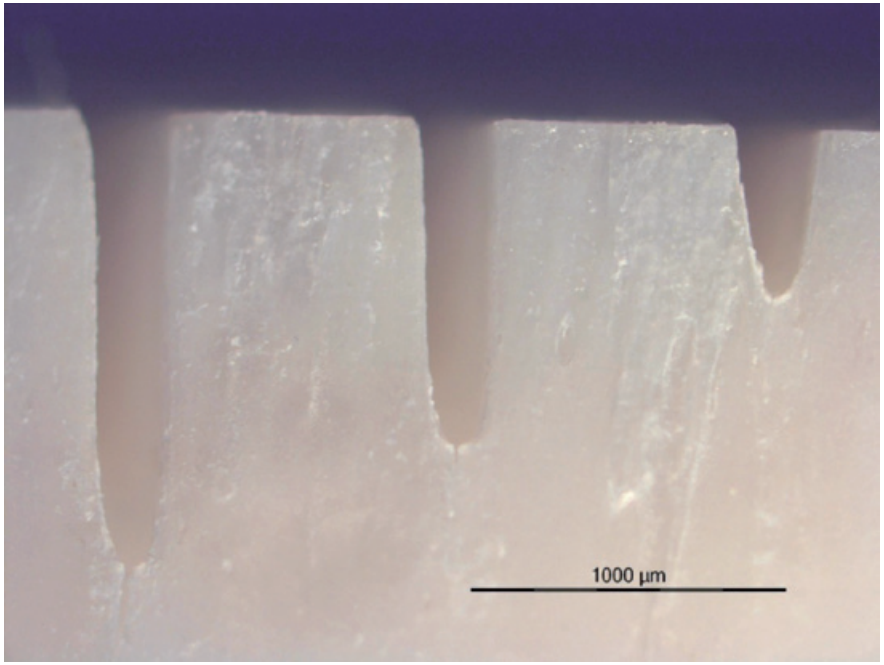
Patient care in our clinic covers the correction of dental malocclusion in children and adults. In collaboration with other departments, we also treat patients with significant dental disproportions, which require both orthodontics and orthognathic surgery, and patients with cleft lip and palate. Furthermore, we are specialized in the diagnosis and treatment of the dental problems of wind instrumentalists.



Smart Dentition developed in cooperation with the Faculty of Engineering of the University of Freiburg. All individual model teeth are equipped with a sensor module for measuring the three-dimensional forces and moments exerted on the teeth by orthodontic appliances. This innovative tool can be used for improving orthodontic strategies and for the training of orthodontists with objective force-moment feedback.

Selected Publications:

- *Schindler HJ, Hellmann D, Giannakopoulos NN, Eiglsperger U. van Dijk JP, Lapatki BG (2014): Localised task-dependent motor-unit recruitment in the masseter. J Oral Rehabil, 41 (7): 477-485.*
- *Radeke J, van Dijk JP, Holobar A, Lapatki BG (2014): Electrophysiological method for examining the muscle fiber architecture of the upper lip in cleft-lip subjects. J Orofac Orthop, 75 (1): 51-61.*
- *Geiger ME, Lapatki BG (2014): Determination of the centre of resistance of individual teeth based on 2D and 3D radiographs. J Orofac Orthop, 75 (2): 96-106.*
- *Rues S, Panchaphongsaphak B, Gieschke P, Paul O, Lapatki BG (2011): An analysis of the measurement principle of smart brackets for 3D force and moment monitoring in orthodontics. J Biomech, 44: 1892-1900.*
- *Lapatki BG, van Dijk JP, van de Warrenburg BPC, Zwarts MJ (2011): Botulinum toxin has an increased effect when targeted toward the muscle's endplate zone: a high-density surface EMG guided study. Clin Neurophysiol, 122: 1611-1616.*



Bone cuts with a novel laser device.

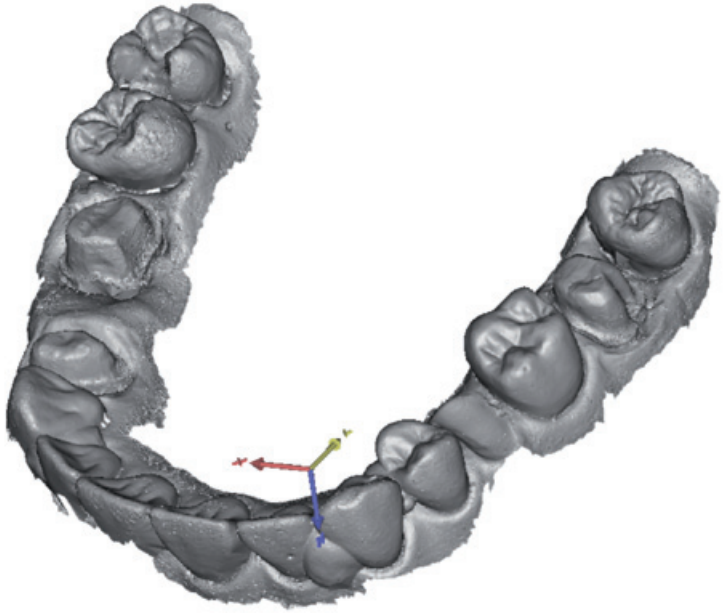
Co-opted:

Institute of Laser Technology in Medicine and Metrology (ILM)

Head of Institute: Prof. Dr. Raimund Hibst
Keywords: Laser | optics | bio photonics | applied research

ILM is an independent institute that is both local to and closely associated with Ulm University. Its mission is dedicated to applied research and the transfer of developed technologies into industrial and medical practice. Its basic financing is supplied by the Ministry of Finance and Economics of Baden-Württemberg and supplemented by annual donations from founder companies. The major part (two thirds) of the budget is acquired by means of various projects. With a further eleven institutions ILM represents the *Innovationsallianz* (Innovation Alliance) Baden-Württemberg. Currently, ILM has roughly fifty employees (including eleven PhD students) in addition to five to ten students. Its annual budget totals approximately four million euros.

From its initial research into laser medicine, ILM has since developed into a much broader institute of applied photonics and optics. Focusing on a set of core competences, applications are multifaceted. They cover medical/dental diagnostic tools and therapeutic systems, such as an optical caries detector and a variety of medical laser systems, optical sensors for fast virus detection, food and tablet analysis, or snow profiling, as well as in-house developments of a photo-thermal tool for material inspection and of optical 3D topography devices for intraoral scanning or industrial metrology. The research spans from solving Maxwell's equations in order to understand light propagation to clinical studies in the institute's day clinic.



Lower jaw scanned with an internally developed intraoral 3D scanner.

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Selected Publications:

- *Jäger, M., Foschum, F. & Kienle, A. 2013, "Computation of the optical properties of turbid media from slope and curvature of spatially resolved reflectance curves," Physics in Medicine and Biology, vol. 58, no. 15, pp. N211-N216.*
- *Kuhn, K., Rudolph, H., Luthardt, R.G., Stock, K., Diebolder, R. & Hibst, R. 2013, "Er:YAG laser activation of sodium hypochlorite for root canal soft tissue dissolution," Lasers in surgery and medicine, vol. 45, no. 5, pp. 339-344.*
- *Liemert, A. & Kienle, A. 2012, "Light transport in three-dimensional semi-infinite scattering media," Journal of the Optical Society of America A: Optics and Image Science, and Vision, vol. 29, no. 7, pp. 1475-1481.*
- *Rothe, T., Schmitz, M. & Kienle, A. 2012, "Angular and spectrally resolved investigation of single particles by darkfield scattering microscopy," Journal of Biomedical Optics, vol. 17, no. 11.*
- *Udart, M., Stock, K., Graser, R. & Hibst, R. 2011, "Inactivation of bacteria by high-power 940nm laser irradiation," Medical Laser Application, vol. 26, no. 4, pp. 166-171.*



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Co-opted:

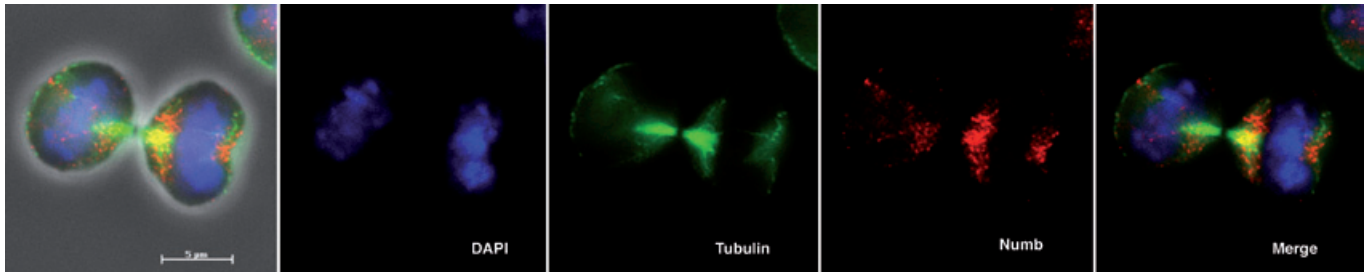
Institute of Psychology and Education

Kolassa Group: Clinical & Biological Psychology
Head of Group: Prof. Dr. Iris-Tatjana Kolassa
Keywords: Trauma | Molecular Psychology | Aging | Post-traumatic Stress Disorder | Genetics

The work group of Clinical and Biological Psychology is part of the Institute of Psychology and Education in the Faculty of Engineering and Computer Science. The team, headed by Prof. Dr. Iris-Tatjana Kolassa, who in addition is a co-opted member of the Medical Faculty, consists of eighteen members: two postdocs; fourteen doctoral students (two from abroad); and one medical technical assistant. 78% of the team are female. The research of the work group focuses on traumatic stress and its molecular consequences, the genetics of Post-traumatic Stress Disorder, psychological and biological factors in the transgenerational cycle of maltreatment, physical exercise and cognitive training in the prevention of cognitive aging, silver gaming and cognition, and electroencephalography in the assessment of indicators of consciousness in brain-injured patients. Furthermore, the team is currently establishing a Psychotherapeutical Outpatient Clinic for the treatment of disorders of the trauma spectrum that is headed by Dr. Roberto Rojas as psychotherapist and supervisor.

Selected Publications:

- *Moreno-Villanueva M, Morath J, Vanhooren V, Elbert T, Kolassa S, Libert C, Bürkle A, Kolassa I-T (2013): N-Glycosylation profiling of plasma provides evidence for accelerated physiological aging in Posttraumatic Stress Disorder. Transl. Psychiatry, 3: e320.*
- *Papassotiropoulos A, Gerhards C, Heck A, Ackermann S, Aerni A, Demougin P, Elbert T, Ertl V, Gschwind L, Hanser E, Huynh K-D, Jessen F, Kolassa I-T, Muhs A, Paganetti P, Spalek K, Vogler C, Pfeifer A, de Quervain D (2013):Human genome-guided identification of memory-modulating drugs. Proc. Natl. Acad. Sci. U.S.A., 110(46): e4369-4374.*
- *Wilker S, Kolassa I-T (2013): The formation of a neural fear network in Posttraumatic Stress Disorder: Insights from molecular genetics. Clin. Psychol. Sci., 1(4): 452-469.*
- *Wilker S, Kolassa S, Vogler C, Thurm F, Elbert T, Papassotiropoulos A, de Quervain D J-F, Kolassa I-T (2013): Resilience to the development of Posttraumatic Stress Disorder predicted by common KIBRA alleles. Biol. Psychiatry, 74(9): 664-671.*
- *de Quervain D J-F, Kolassa I-T, Ackermann S, Aerni A, Boesiger P, Demougin P, Elbert T, Ertl V, Gschwind L, Hadziselimovic N, Hanser E, Heck E, Hieber P, Huynh K-D, Klarhöfer M, Luechinger R, Rasch B, Scheffler K, Spalek K, Stippich C, Vogler C, Vukojevic V, Stetak A, Papassotiropoulos A (2012): PKCα is genetically linked to emotional memory in healthy Europeans and to the risk for PTSD in heavily traumatized Rwandese. Proc. Natl. Acad. Sci. U.S.A., 109(22): 8746-8751.*



Aging of hematopoietic stem cells (HSCs) is associated with impaired hematopoiesis in the elderly. Despite a large amount of data describing the decline of HSC function upon aging, the molecular mechanisms of this process still remain largely unknown and this therefore precludes rational approaches to attenuate stem cell aging. The figure shows the analysis of mode and outcome of LT-HSCs division upon aging: symmetric and asymmetric divisions are observed.

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Co-opted:

Institute of Molecular Medicine, Stem Cells and Aging

Head of Institute: Prof. Dr. Hartmut Geiger

Keywords: Stem cells | regeneration | aging | molecular medicine | hematopoietic

Adult stem cells are a powerful source in tissue regeneration as well as in cancer. How adult stem cells are regulated in health, disease and aging is still not very well understood. The Geiger lab at the Institute of Molecular Medicine, Stem Cells and Aging investigates the role of stem cells in tissue regeneration and aging, and translates the findings into procedures that may lead to improved treatment of tissue degeneration and also aging. In the laboratory, where our primary focus is on blood forming (hematopoietic) stem cells, we ask the following questions:

- Does the stem cell itself contribute to changes in its phenotype or is the niche the driving force?
- How do normal stem cells become malignant stem cells?
- Is the aging of stem cells a common theme and, based on our knowledge, can we develop pathways that revert aging?
- Can we attenuate the steps that lead from a normal to a malignant stem cell?
- Where do stem cells reside and why?

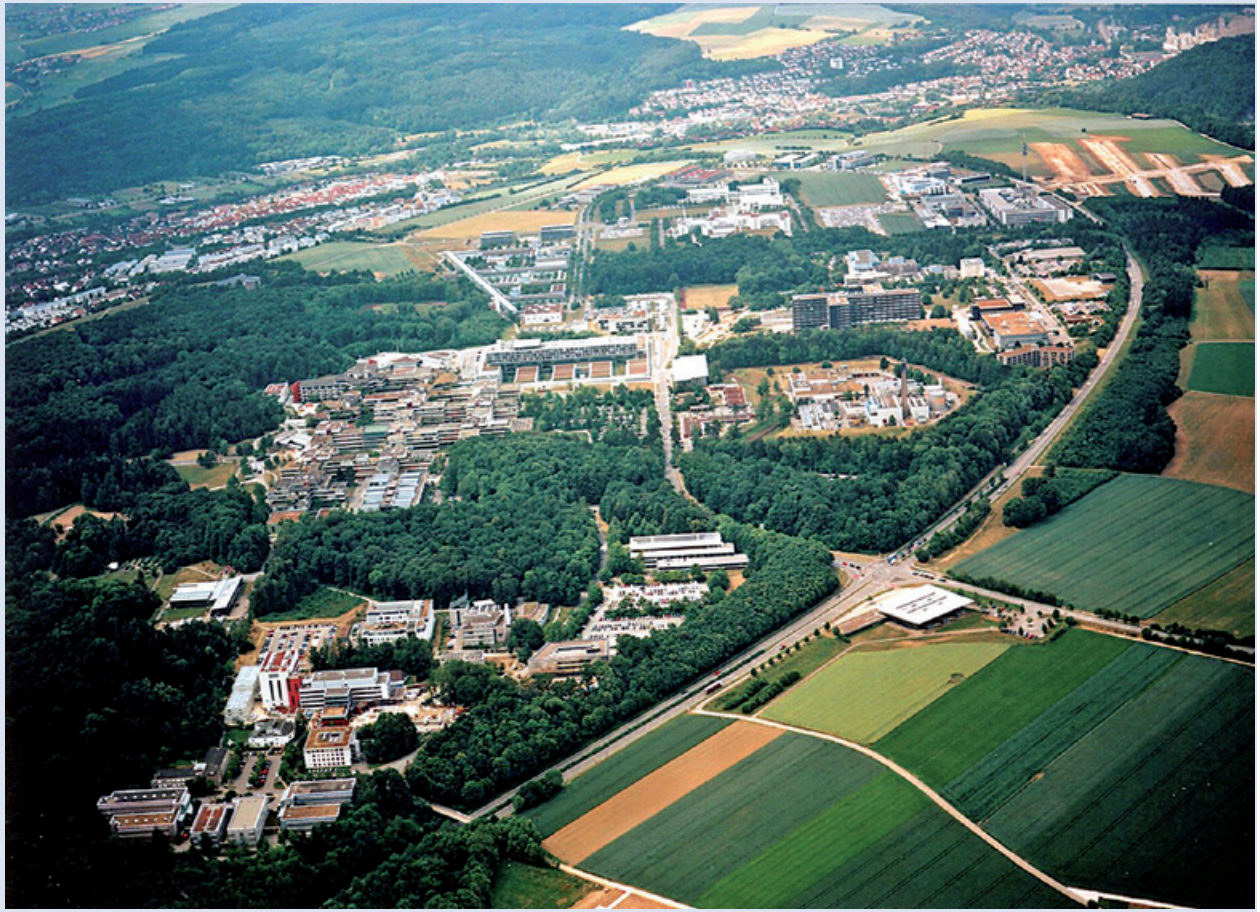
These are the questions which we are seeking to answer in the Geiger lab.

Selected Publications:

- *Florian MC, Dorr K, Niebel A, Daria D, Schrezenmeier H, Rojewski M, Filippi MD, Hasenberg A, Gunzer M, Scharffetter-Kochanek K, Zheng Y, Geiger H (2012) Cdc42 activity regulates hematopoietic stem cell aging and rejuvenation. Cell stem cell 10: 520-530.*
- *Geiger H, Pawar SA, Kerschen EJ, Nattamai KJ, Hernandez I, Liang HP, Fernandez JA, Cancelas JA, Ryan MA, Kustikova O, Schambach A, Fu Q, Wang J, Fink LM, Petersen KU, Zhou D, Griffin JH, Baum C, Weiler H, Hauer-Jensen M (2012) Pharmacological targeting of the thrombomodulin-activated protein C pathway mitigates radiation toxicity. Nat Med 18: 1123-1129.*
- *Vas V, Wandhoff C, Dorr K, Niebel A, Geiger H (2012) Contribution of an aged microenvironment to aging-associated myeloproliferative disease. PLoS ONE 7: e31523.*
- *Florian MC, Nattamai KJ, Dorr K, Marka G, Uberle B, Vas V, Eckl C, Andra I, Schiemann M, Oostendorp RA, Scharffetter-Kochanek K, Kestler HA, Zheng Y, Geiger H (2013) A canonical to non-canonical Wnt signalling switch in haematopoietic stem-cell ageing. Nature 503: 392-396.*
- *Geiger H, de Haan G, Florian MC (2013) The ageing haematopoietic stem cell compartment. Nat Rev Immunol 13: 376-389.*



Facts and Figures



The Campus Oberer Eselsberg, Ulm University 2014.



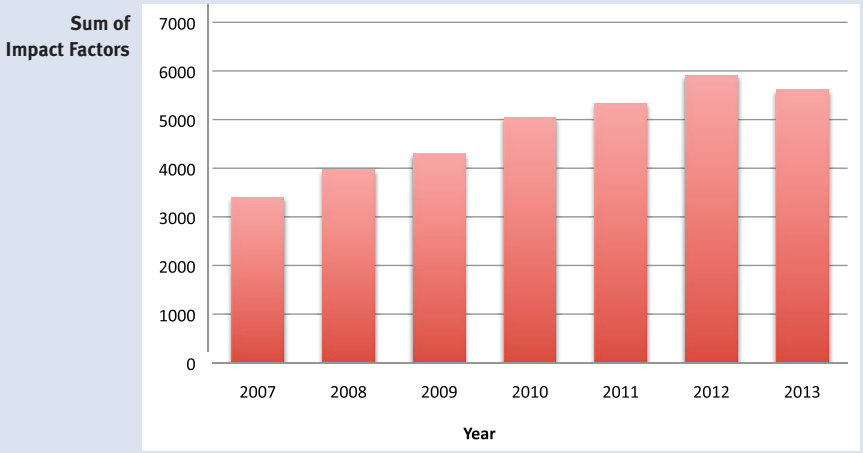
Ulm as an economic center in the south of Germany

Ulm and its sister city Neu-Ulm are the economic center of a large region that lies between the Alb and Lake Constance. Approximately 180,000 people live in both cities and almost 1,000,000 inhabit the region of Danube-Iller. Approximately 17,500 young people study in Ulm and Neu-Ulm. There are over 10,000 businesses from diverse areas and branches of industry, among which are such enterprises with a world-wide reputation as Iveco-Magirus (Commercial Vehicles), Evo-Bus (Buses), Airbus Defence and Space, Ratiopharm/Merckle (Teva Group; Pharmaceutical Industry), Gardena (Husqvarna Group; Gardening Tools), Ulrich (Medical Technology), Takata (Vehicle Security Systems), Liqui Moly (Automotive Service) and the Daimler Science Center. Today, there are approximately 120,000 employment opportunities in Ulm and, with some 9,350 employees, Ulm University has become the city's largest employer.

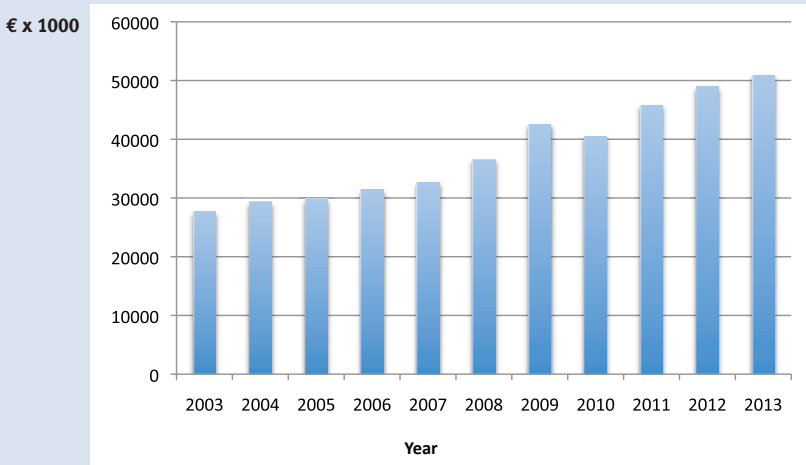
Ulm University Medicine – a motor that drives the dynamic development of the greater Ulm area

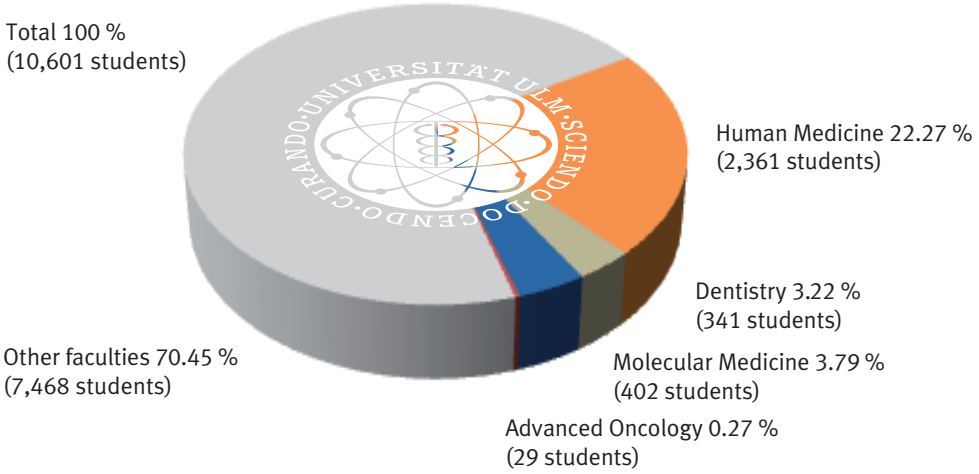
The rapid industrial and scientific development of our city has not remained unnoticed outside Ulm. The well-known journal *Capital* writes: "... In recent years, Ulm has pursued a technology policy that has become exceedingly successful. Modern service and research facilities as well as attractive scenic surroundings promise further dynamic developments for real estate." According to the Institute of the German Economy (IW): "Today, Ulm as a job market is among the top performing cities in Germany. In the ratio of registered citizens to the number of employees subject to social security contributions, Ulm has reached fourth place." In addition to this, the *Handelsblatt* attests to the innovative economic and structural policy of the city of Ulm: "Ulm is one of the *silent stars* and one of the regions in Germany with the greatest growth potential." Ulm University Medicine is also one of the motors that has helped to drive this development. For instance, third-party funding has increased by some 300% in the last 17 years from €15.2 million in 1996 to €50.9 million in 2013 while the number of people employed by means of this funding has increased from 681 to 930 in the last four years.

Sum of Impact Factors of Papers Published by Scientists of Ulm University Medicine



Development of External Funds Revenues





Proportion of students enrolled in the Faculty of Medicine relative to the total number of students at Ulm University. (Study year 2013/2014)

Examinations at Ulm

In a recent evaluation by the IMPP (Institute for Medical and Pharmaceutical Examination Questions), which analyses the outcome of the written part of the first section of the medical examination, Ulm University Medicine was placed in fifth position out of 33 German faculties. The students achieved above-average results in all subjects (physics, physiology, chemistry, biology, anatomy, psychology and sociology).

In 2014, 257 students at Ulm University undertook the final national board examination in Human Medicine. The results of this examination were comparative to the nationwide average of 237.74 out of a maximum of 314 accessible points. Around half of all students studying Human Medicine complete their studies over an average period (*Regelstudienzeit*) of twelve semesters. In Germany, the average final mark of graduates based on the results of a written and an oral examination varies between “well” and “adequate.” Graduates of Dentistry and Molecular Medicine on average attain “good” results.

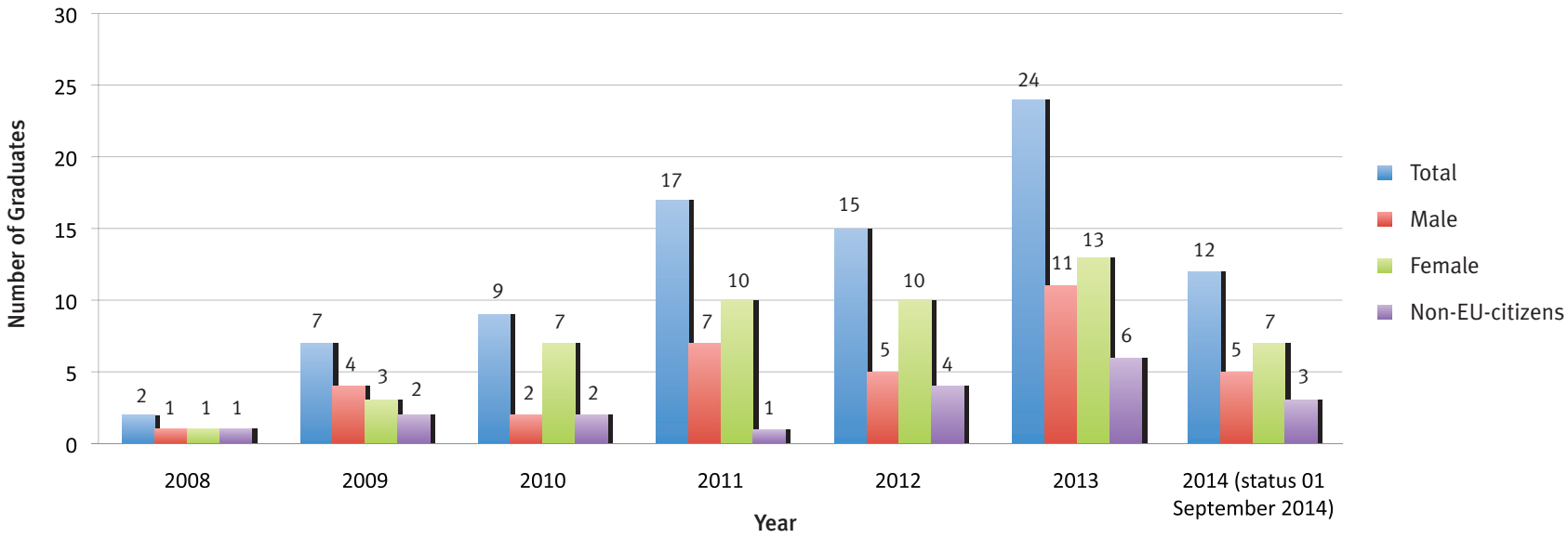
http://www.impp.de/IMPP2010/pdf/ErgMedM1H14.pdf; entnommen am 22. September 2014
Destatis, 2012: https://www.destatis.de/DE/Publikationen/Thematisch/BildungForschungKultur/Hochschulen/BroschuereHochschulenBlick0110010137004.pdf?__blob=publicationFile; entnommen am 22. September 2014

Student Statistics

Since the academic year of 2007/2008, the Medical Faculty at Ulm has registered a total number of students that has increased by 17.4% up to the academic year of 2013/2014. According to a forecast relating to demographic changes in Ulm, the proportion of inhabitants between the ages of 18 and 35 will steadily increase year by year. As a result of this, Ulm will eventually be designated a university city and will have to adapt to the needs of this younger generation.

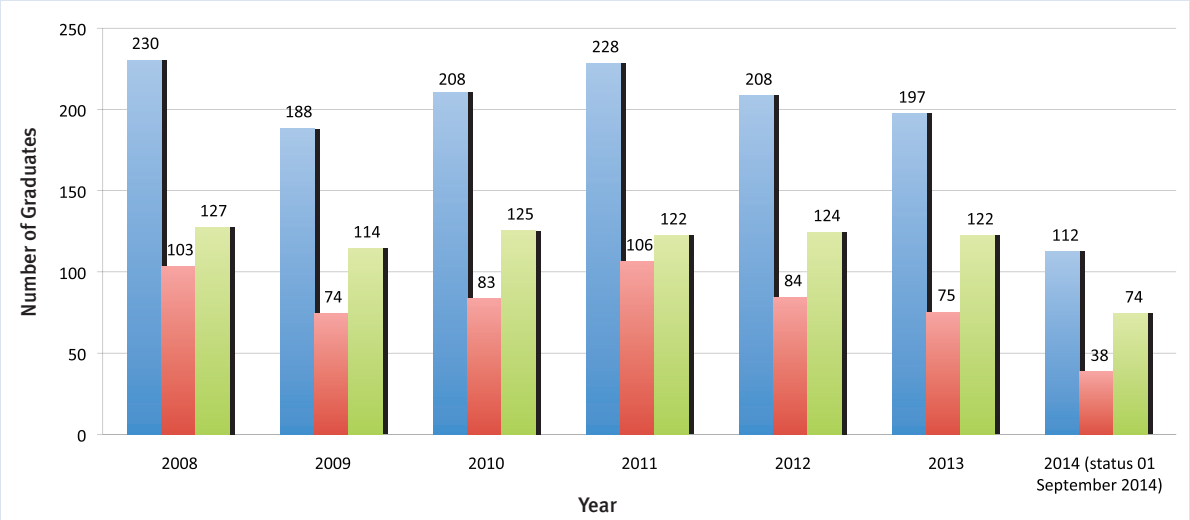


Number of Graduates – Dr. rer. nat. and PhD – from the International Graduate School in Molecular Medicine Ulm 2008-2014

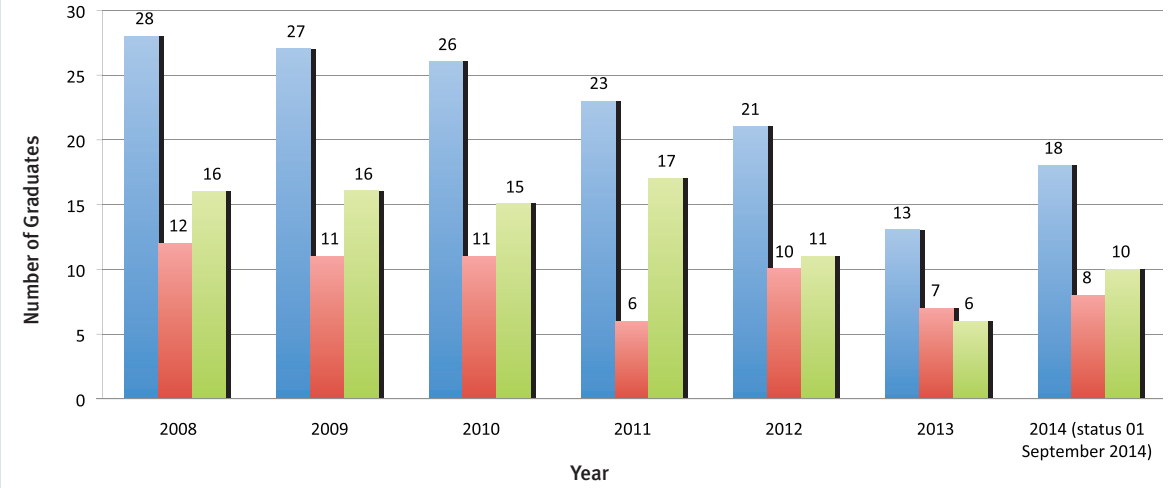




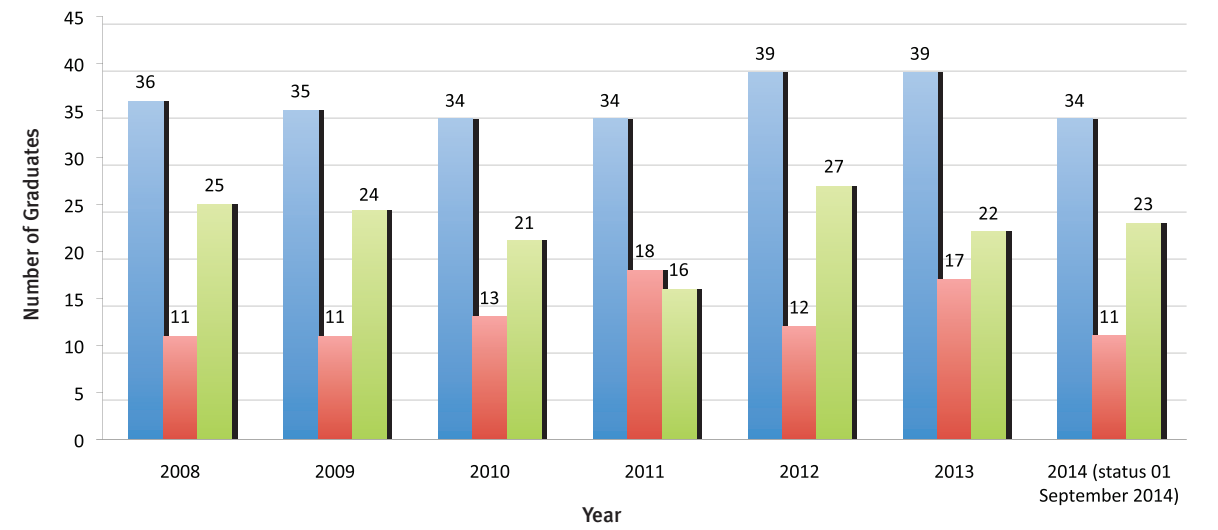
Number of Graduates – Dr. med. – 2008-2014



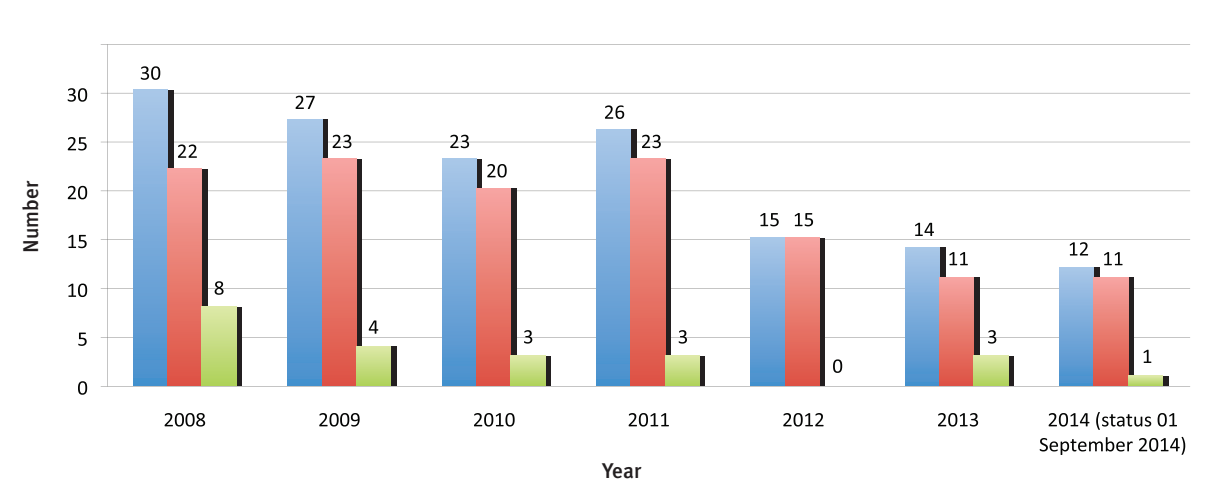
Number of Graduates – Dr. med. dent. – 2008-2014



Number of Graduates – Dr. biol. hum. – 2008-2014



Postdoctoral Lecture Qualifications (*Habilitationen*) 2008-2014





Medical Faculty and Ulm University Medical Center

Statistical data

Patients	
Outpatient cases (2013)	238,272
Inpatient cases (2013)	46,274
Day patient cases (2013)	2,949

Departments and Institutes	
Clinical departments	28
Clinical departments with the participation of external institutions	5
Clinical-theoretical institutes	11
Preclinical institutes	10

Employees	
Total employees (July 2014)	7,453
Physicians	874
Nurses	1,604
Technical-medical staff	2,009

Ulm University Medical Center

Ulm University Medical Center is dedicated to providing excellent health care to our patients. Our clinical and scientific experts strive daily to gain a better understanding of human disease and to discover more effective treatments. Scientists and clinicians work closely together and transfer new scientific insights quickly from lab to bench by offering patients constantly improved diagnostic and treatment options. In addition to our in-hospital services, Ulm University Medical Center also administers a number of treatment options in our outpatient departments.

High standards of medical care are guaranteed by our renowned professors, our distinguished physicians and our skilled nursing staff. Ulm University Medical Center is committed to attracting highly qualified physicians and health care professionals and is dedicated to providing them with continuous support and training. We complement their expertise by investing in state-of-the art equipment and technology to provide excellent medical care. Furthermore, our experienced management staff ensures ongoing improvements in high quality health care through regular reviews of professional standards and clinical treatment procedures with the aim of improving patient safety and monitoring patient satisfaction.

Diagnostic and therapeutic decisions are based on a comprehensive approach to health care. To strengthen our commitment to multidisciplinary patient care, Ulm University Medical Center encourages the formation of comprehensive care centers. Our Comprehensive Cancer Center Ulm (CCCU) is funded by the *Deutsche Krebshilfe* (German Cancer Aid) as a center of excellence. Within the CCCU our clinicians and scientists enjoy the finest international reputation due to, for example, their innovative treatment of patients suffering from leukemia and lymphoma. In 2012, the Center for Rare Diseases (ZSE – *Zentrum für seltene Erkrankungen*) was founded as part of a nationwide network.



Ulm University Medical Center functions interdependently and in cooperation with the Medical Faculty of Ulm University. Our joint mission is to teach and train medical students to ensure the highest quality of expertise for our future physicians and scientists. We are also proud of the present high standard of teaching and training that our academy of health care professionals provides to our prospective nursing and laboratory staff.

Ulm University Medical Center currently encompasses two main hospital locations and two other satellite locations in Ulm, and is complemented by cooperating facilities in the region. In 2012, our new Center for Surgery came into operation and is located at Ulm Science Park within the immediate vicinity of a wide range of other departments, including the Center for Internal Medicine. This arrangement enhances our multidisciplinary approach to excellence in patient care, clinical and laboratory research, and our teaching practices and training. The new Center for Surgery pools the internationally renowned expertise of our clinicians and scientists in the field of traumatology. Ulm University Medical Center provides an extensive range of resources through its cooperation with other hospitals, research organizations, rehabilitation facilities, general practitioners and specialists, social institutions and self-help groups. In addition, we offer active programs in education, community outreach, prevention and control.

We are committed to providing excellent comprehensive health care for the people of the region and beyond by combining outstanding medical competence with a dedication that is both perceptible and compassionate.

Imprint

Publisher
Ulm University Medicine

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2015

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We cordially thank the institute and department directors as well as all employees of the Medical Faculty and Ulm University Medical Center for their support.



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