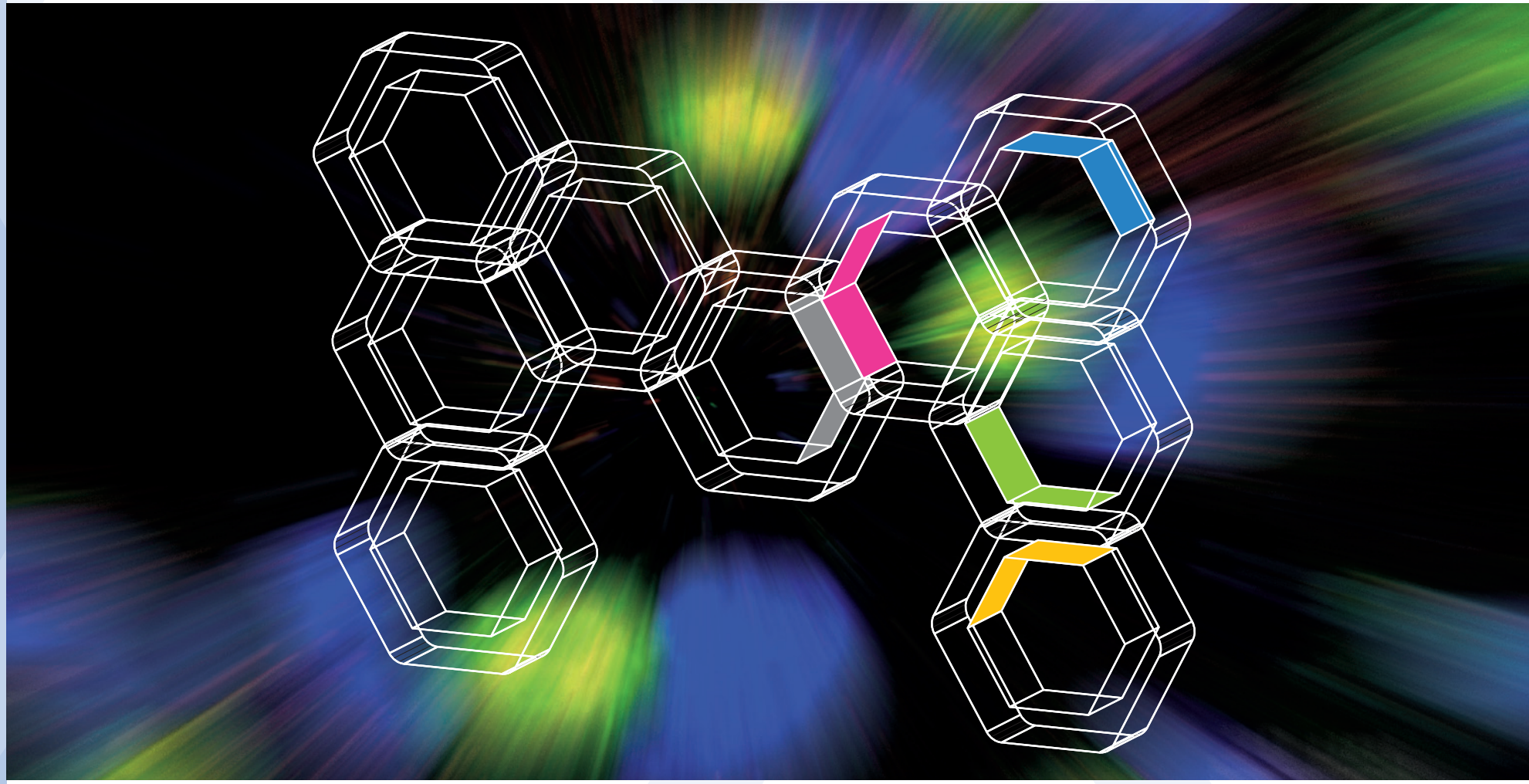
ulm university universität
uulm



International Graduate School in Molecular Medicine Ulm
Biannual Report 2016

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

IGradU

Former Board of Directors: B. Knöll, M. Kühl, D. Brockmann, T. Weil, A. Gross

Welcome to the information brochure of the International Graduate School in Molecular Medicine Ulm!

Ten Years! It is hard to believe that the International Graduate School in Molecular Medicine (IGradU) was already founded ten years ago in 2006. This jubilee is a good reason to let us look back and summarize the most important and innovative achievements and programs that IGradU has established. Starting with only seven PhD students, who entered the International PhD programme in Molecular Medicine in 2005 and who have been funded by scholarships from the Medical Faculty of Ulm University, we are currently training 205 PhD students and 34 medical students as well as serving 118 alumni. Since 2007, IGradU has been funded as one out of 45 Graduate Schools within the framework of the Excellence Initiative of the German federal and state governments. We consider this funding as a special recognition of our motivation, our work and of our innovative training concepts. We would also like to mention that running such an institution as the Graduate School would not be possible without the ongoing intellectual and financial support of the Medical Faculty and Ulm University. In this respect, we would cordially like to thank all the boards of the University involved in this support.

What are our most important achievements and programs? We have established six Research Training Groups dealing with different topics in Molecular Medicine. Each PhD student is supervised by a Thesis Advisory Committee consisting of at least three members, one of whom comes from abroad. We are the umbrella organization for the training of PhD students from a large variety of collaborative

research centers funded, for instance, by the German Research Organisation (DFG) or the Federal Ministry of Education and Research (BMBF), such as the CRC1149 – *Danger Response, Disturbance Factors and Regenerative Potential after Acute Trauma, CRC1074 – Experimental Models and Clinical Translation in Leukemia, and SyStaR – Molecular Systems Biology of Impaired Stem Cell Function and Regeneration during Aging*, to mention just a few. We have enhanced our internationalization strategy by establishing joint PhD programs with the University of Padua, Italy, and the University of Oulu, Finland, as well as expanding our guest professor program. For instance, Prof. Philip Wong, Baltimore, was appointed as a long-term guest professor in 2014 and is the successor of Prof. Hiromitsu Nakauchi, Tokyo. Prof. Wong established a very successful junior research team working on animal models of neurodegenerative diseases. We have also implemented a diversity of gender programs to support PhD students with children or female students during pregnancy. We are running different mentoring programs, including the well-known M4M-program (Mentoring for Molecular Medicine) in which senior citizens of Ulm offer support for our students and especially for those from abroad so that, from the time of their arrival in Germany until their disputation, these mentors can help to facilitate their integration into German society and culture. In addition, we have very recently established a Junior Faculty to promote the scientific career of young postdocs.

How do we measure the success of our training programs as well as that of the Graduate School? Of course, publications are only one side of the coin and our students generally publish three to four papers in international peer-reviewed journals while completing their thesis. However, their future life and scientific career are of even more importance to us. We are proud that our alumni continue their career in well-known and highly ranked scientific institutions such as Harvard Medical School (USA), Stanford University School of Medicine (USA), Johns Hopkins (Baltimore, USA), McGill University (Canada), ETH Zürich (Switzerland) or *Deutsches Krebsforschungszentrum* DKFZ (Germany). Moreover, international global pharmaceutical players, such as Boehringer Ingelheim and Roche, are also highly interested in our graduates.

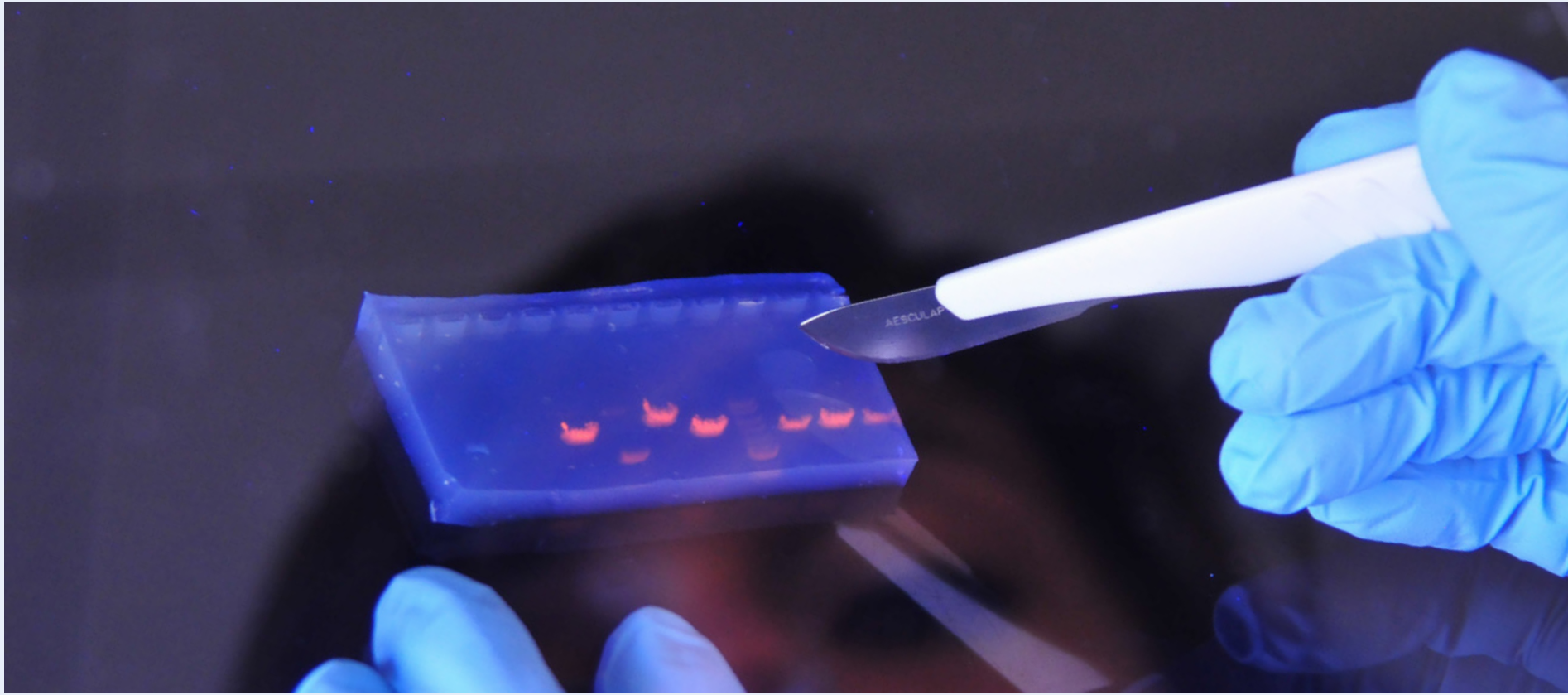
We hope you enjoy reading our biannual report of 2016.

On behalf of the Board of Directors,

Current Board of Directors: B. Knöll, D. Brockmann, T. Weil, J. Ankerhold, M. Kühl

Prof. Dr. Michael Kühl
Chairman

PD Dr. Dieter Brockmann
Managing Director



The Graduate School

Molecular Medicine – the challenge of the 21st Century

What is Molecular Medicine?

The discovery of microorganisms as the cause of infectious diseases and penicillin as an effective weapon to combat them revolutionized the field of medicine in the last century. It soon became clear that the causes of many human diseases reside in the cells, namely, the genes and the proteins they produce. Research in the life sciences has been revolutionized in recent years by the introduction of 'omics technologies, advances in imaging technologies, the development of genome-editing tools such as CRISPR/CAS, as well as by applying computer science technologies to life science problems in systems biology. To broaden this knowledge and its use for the well-being of patients is the aim of the interdisciplinary scientific subject of *Molecular Medicine* or Biomedicine. Scientists working in the field of Molecular Medicine analyze the molecular mechanisms of the origin of diseases 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, cancer and 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 increase the costs for our healthcare systems dramatically, especially in view of the dramatic demographic changes in population structure. Because of the significance of Molecular Medicine for modern day society, the need to provide highly trained scientists is of immense importance.

PhD training in Molecular Medicine at Ulm University

Modern concepts in Molecular Medicine utilize interdisciplinary approaches that combine methods from the fields of molecular biology and genetics with those from informatics, mathematics, physics and engineering. In the past, PhD studies in Germany lasted many years and were marked by a strong dependency on one scientific supervisor. Today's training concepts are based on a well-structured and defined schedule with a broader approach to supervision. In October 2005, the Medical Faculty of Ulm University launched a three-year doctoral training program entitled *International PhD Programme in Molecular Medicine*. The major aims of this program are:

- to improve graduate training by creating an active and motivating research environment
- to encourage graduates to perform independent scientific research by adopting a transdisciplinary approach, incorporating international supervision and mentoring
- to steer graduate education by establishing a distinctive program structure
- to advance graduate career opportunities in the academic world and in industry.

Our *International PhD Programme in Molecular Medicine* leads to the international degree of *Doctor of Philosophy* (PhD) or the German degree of *Doctor rerum naturalium* (Dr. rer. nat.). Each PhD student is assigned an interdisciplinary Thesis Advisory Committee (TAC) consisting of scientists from Ulm University and abroad to offer scientific advice from a wide range of perspectives. The graduates perform their research in the different institutes of Ulm University and come together for common training activities, and to attend optional courses organized by the Graduate School. During the three-year program, the students complete two intermediate evaluations before their TAC and international experts to ensure appropriate progress in their scientific project.

Training in clinical research

To strengthen the training of medical students in clinical research, the Graduate School also runs the program *Experimental Medicine*. In order to participate in this program, students of human medicine are obliged to interrupt their course of studies for nine months to work full time in a laboratory. During this period, students are supported by a fellowship of the Medical Faculty or the Graduate School. Besides their lab work, doctoral students must attend seminars, prepare literature reports and give progress reports. These initiatives have significantly increased the quality of medical dissertations at Ulm University as documented by the final grade and the number and quality of publications in peer-reviewed journals. At the same time, medical students are thus excellently prepared for PhD training.

Proven excellence

In 2006, the *Molecular Medicine* study programs at Ulm University were integrated into the newly founded *International Graduate School in Molecular Medicine Ulm*. One year later, the school's training concept received official recognition of its excellence through funding from the Excellence Initiative of the German federal and state governments amounting to €1 million per annum for a period of five years. We have been subsequently able to secure this funding until 2017 with an amount of €1.5 million per year. This *Excellence Initiative* was initiated in 2005 to grant competitive awards to the best performing German universities and has subsequently proved to be a great success for our Graduate School, the Medical Faculty and Ulm University. The PhD program was accredited and re-accredited (in 2015) by the "Central Evaluation and Accreditation Agency Hannover" *(ZevA, Zentrale Evaluations- und Akkreditierungsagentur Hannover)*. This is yet another endorsement of the high scientific and educational quality of the program we offer.

Leitmotif of IGradU

It is the vision and declared objective of IGradU to train PhD and MD students in an international context to an excellent standard of quality and thereby to strengthen the scientific performance of Ulm University in the field of Molecular Medicine and to further develop its national and international reputation.

Promotion of Junior Scientists

The Graduate School is committed to the promotion of junior scientists and offers a variety of compatible programs in order to support and actively encourage junior scientists.

The International PhD Programme in Molecular Medicine

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

In October 2005, the Medical Faculty of Ulm University launched a three-year doctoral training program entitled *International PhD Programme in Molecular Medicine*. This postgraduate course offers a structured doctorate conducted in English. The course was accredited in March 2009 and re-accredited in 2015. During their postgraduate course, doctoral candidates are monitored by a Thesis Advisory Committee (TAC) of three members. The TAC consists of scientists from Ulm University and abroad and offers scientific advice from a wide range of perspectives. A member of the Junior Faculty can act as a fourth member of the TAC. This is a chance for Junior Faculty members to have their first experience in advising PhD students. The graduates perform their

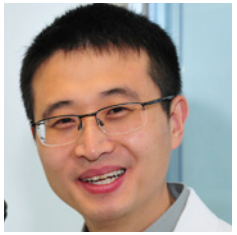
research in the various institutes of Ulm University and come together for common training activities and courses organized by the Graduate School. Each student's coursework is calculated and accredited according to the European Credit Transfer and Accumulation System (ECTS). After having successfully defended their thesis, graduates opt to receive either the international academic title of PhD or the German academic title Dr. rer. nat. The opportunity for graduates 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.

Recently, the International PhD Programme in Molecular Medicine was extended to include a joint PhD program with either the University of Padua, Italy, or the University of Oulu, Finland. To obtain a joint degree, candidates must stay for at least six months at the host university. Moreover, one of the TAC members must also be from Padua or Oulu. The establishment of such joint degree programs is part of the internationalization strategy of IGradU.

GRK 1789 Cellular and Molecular Mechanisms in Aging

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

CEMMA is a research training program for graduate students that focuses on aging research. Demographic developments predict a significant increase in age-associated diseases. Thus, age-associated diseases and their prevention will become a central aspect of medicine, business and social studies. Improved in-depth knowledge on basic molecular and cellular mechanisms of aging will allow the designing of rational approaches and therapies that are ultimately aimed at achieving healthy aging. The research training program of Cellular and Molecular Mechanisms in Aging (CEMMA) will recruit and train the next generation of scientists in aging research, a very critical task in light of anticipated demographic developments. The qualification program with respect to aging research includes distinct teaching modules on model systems in aging research and on theories on molecular aging in addition to modules analyzing aging with respect to general medicine and social studies. Research projects within CEMMA focus on aging and cancer, stem cells, DNA-repair, age-related changes in immune cells and inflammation, and neurodegenerative diseases.



Zeguang Wu
Born in 1983, he obtained his master's degree in Clinical Medicine in China. He joined the International Graduate School in Molecular Medicine Ulm in 2011 and performed research for his PhD thesis at the Institute of Virology, Ulm University Medical Center. He continued his postdoctoral research at the same institute after his graduation in the fall of 2014.
My research focuses on the role of natural killer cells in human cytomegalovirus infection. In November last year, I completed my doctoral dissertation which was entitled, "Natural Killer cells are effectors of the adaptive antiviral immunity and control human cytomegalovirus transmission in vitro."
In my opinion, PhD study is an important period of training for junior researchers. A PhD student requires the ability to learn how to plan a project, to perform experiments and to present results in the manner of a professional scientist. From this point of view, scientific communication with one's peers is critical and it is this that I have most benefitted from during my time at the International Graduate School in Molecular Medicine Ulm. The Graduate School offers a series of lectures by senior researchers, progress reports based on individual topics of research, seminars presented by invited speakers, independent Spring and Fall Meetings, and financial support to attend conferences. These great opportunities help students to present and communicate the latest findings of their research. I am also grateful to the availability of family support and childcare programs specifically intended for parent students. These programs are an enormous benefit to many parents in a variety of situations.

Cooperative PhD Training Group – Pharmaceutical Biotechnology (PBT)

Speakers: Prof. Dr. Peter Dürre, Institute of Microbiology and Biotechnology;
Prof. Dr. Jürgen Hannemann, University of Applied Science in Biberach

The region around Ulm is the second largest pharmaceutical industry area within Germany. Prominent members are Boehringer Ingelheim Pharma GmbH in Biberach, Rentschler Biotechnologie GmbH in Laupheim, and Ratiopharm/Teva Pharmaceutical Industries in Ulm. The field of Pharmaceutical Biotechnology is an interdisciplinary research topic rooted in both the natural sciences and medicine, and is therefore optimally suited for a cross-university cooperative PhD Training Group. The cooperative PhD Training Group includes research projects which cover the whole valued added chain in the field of Pharmaceutical Biotechnology. Through its specifically designed program, the PBT enables an especially qualified degree with the intensive cooperation and interlinking of the two universities in the field of the life sciences. The PhD Training Group of Ulm/Biberach is one of eight cooperative PhD Training Groups that have been funded by the State of Baden-Württemberg since 2011. After re-evaluation in 2014, the funding by the state of Baden-Württemberg was extended until 2017. The scholarship holders are chosen in a common selection procedure with the International Graduate School in Molecular Medicine Ulm and take part in its program.

Study Programme Experimental Medicine

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

In order to combat deficiencies in the supervision and quality of medical theses and to excellently prepare medical students for a career as clinician scientists, the Medical Faculty implemented in 2005 the structured training program *Experimental Medicine* for students following courses of studies in human medicine and dentistry. This training program 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 30 stipends yearly. 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*. As an option, students may attend part of the training programs offered by the *International Graduate School in Molecular Medicine Ulm*.

The Junior Faculty at Ulm University

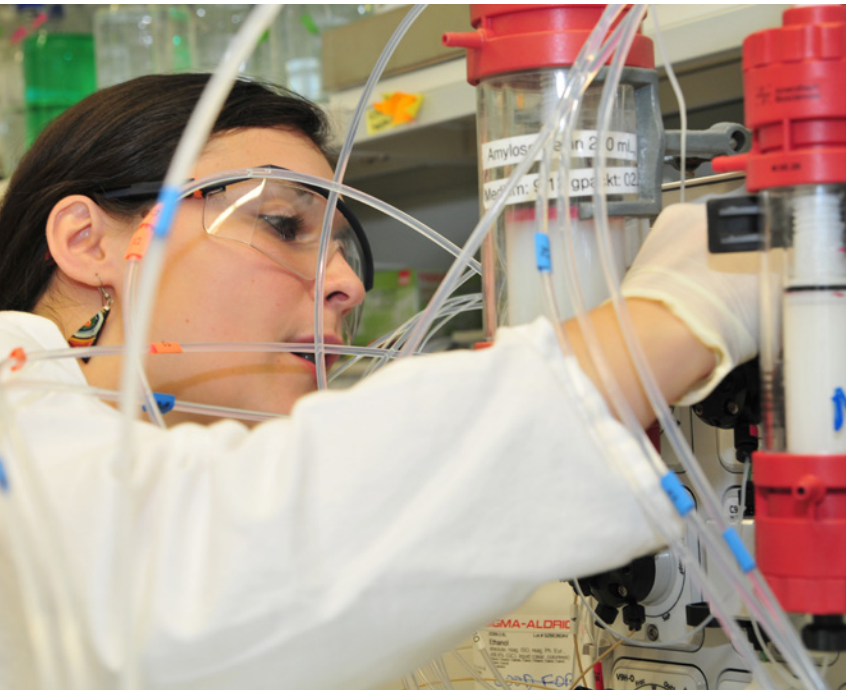
The Junior Faculty (JF) at IGradU is a specific program for junior researchers working at Ulm University or Ulm University Medical Center. A "junior researcher" is a person who has recently completed his/her (PhD) studies and is on the way to establishing his/her own junior research group with the aim of becoming a junior professor and of eventually receiving habilitation.
The overall aim of the Junior Faculty is to promote the careers of junior scientists through active interaction with the university, the faculty boards and society in general. Joining the Junior Faculty offers the following benefits:

- The opportunity to conduct PhD supervision as a member of TAC (Thesis Advisory Committee)
- Supervisors' support
- Opportunities to receive financial support for further/continuing education
- Opportunities to receive travel grants to international conferences
- Mentoring (gender programs, dyadic mentoring, peer-to-peer mentoring)

To become a member of the Junior Faculty, a grant or secured extramural funding is required from, for example, BMBF, DFG, EU Programs, Programs of the Medical Faculty of Ulm University or from state programs such as the Margarete von Wrangell Habilitation Program for women etc. In addition, it is expected that candidates will have already published paper(s) in peer-reviewed international journal(s). Activities of the Junior Faculty comprise continuing education courses according to the wishes of participants, for example, lab management courses, support for pedagogic workshops, the "Teaching Certificate of the State of Baden-Württemberg" as well as participation in the annual science fairs and JF-meetings.

Simon Fischer has a postdoctoral position in the Department of Biopharmaceutical Process Development at Boehringer Ingelheim Pharma GmbH & Co.KG in Biberach, Germany. He graduated in October 2015.

"I am grateful to the International Graduate School in Molecular Medicine Ulm for providing me with a professional environment throughout my entire PhD studies. Generally speaking, the program substantially supports young and motivated students to develop into professional scientists who will eventually be well prepared for a successful career, both in academia and industry. It is especially valuable when you begin as a graduate student that you and your fellow students are guided in the right way from the very beginning. Annual intermediate examinations also enable students to engage more fully by reporting on a regular basis their personal scientific achievements to supervisors. In this way, they learn how to present results in a condensed scientific format, not only to keep supervisors updated but also to receive feedback in return. In addition to this, I would also like to emphasize the fact that the Graduate School requires and also financially supports students so that they can actively attend international conferences. This is clearly a great bonus since it helps students to establish a network with other scientists in their field and this has nowadays become indispensable for the purposes of research. Finally, I would also like to mention that there was a very amusing excursion to the Oktoberfest when PhD students were given the opportunity to meet each other to encourage interdisciplinary exchanges outside the university campus. This event especially helped us, the IGradU members from Biberach, who do most of our work at the Institute of Applied Biotechnology (IAB)."



Else Kröner-Forschungskolleg Ulm – Support for the Scientific Career Development of Junior MDs

Since the spring of 2011, the *Else Kröner Fresenius Stiftung* has funded the research college on the topic of "Stem Cells, Aging and Malignant Transformation – from experimental model to clinical application" in the context of the structured educational program for junior and outstandingly talented clinicians at the Medical Faculty of Ulm University.

Malignant transformation is associated with aging and it is presumed that section-specific stem cells or cancer-initiating stem cells are also involved. Therefore, innovative and promising approaches to successful treatment require a clinical and interdisciplinary way of thinking that involves an interaction of these subject areas. Thus, the findings of the molecular basis of diseases gained in the laboratory can be transmitted to clinical therapies. Junior clinicians have been using their talent in scientific research by transferring it to clinical application and are thus promoting this development of innovative and forward-looking approaches to biomedical therapy. With the help of the *Else Kröner-Forschungskolleg Ulm*, these clinicians are not only given the appropriate freedom to conduct scientific research but also receive the training and mentoring they require according to a sustainable concept. This involves returning to the clinic, continuing the laboratory project, interlinking with clinical work, and being integrated into the rotation and specialist medical training after one or two years of release.
The college is headed by Professor Dr. Stephan Stilgenbauer, Department of Internal Medicine III, and Prof. Dr. Hartmut Geiger, Institute of Molecular Medicine, in close cooperation with PD Dr. Dieter Brockmann, Medical Faculty, Head Division of Science and Research and Managing Director of the International Graduate School in Molecular Medicine Ulm.

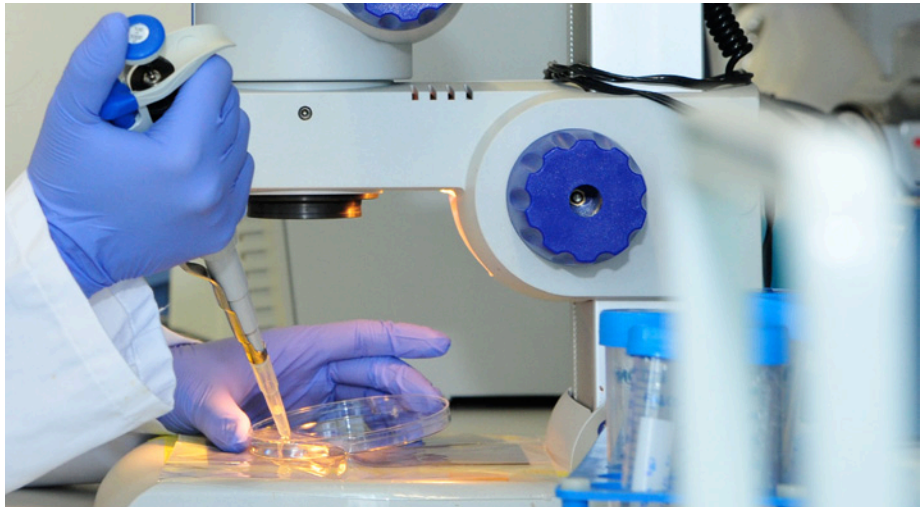
In particular, the program comprises:

- Rotation positions (100% release from clinical obligations) for up to two years
- Experimental work focusing on stem cells, aging and malignant transformation
- A dedicated mentoring and training concept
- Individualized support for a combined scientific and clinical career as a "physician-scientist"

Hertha Nathorff Program of the Medical Faculty – New Impetus for Funding Junior Female Scientists in Biomedical Research

Since May 2013, the Medical Faculty of Ulm University in cooperation with the International Graduate School in Molecular Medicine Ulm supports five talented junior female doctors per year as part of the Hertha Nathorff Funding Program. This program enables the scientific career development of junior female scientists who have a PhD but lack the qualification of a university lecturer. Through 100% release from clinical obligations, junior female scientists can conduct research preferably in the area of experimental investigations but also in clinical investigations. At the same time, medical technical assistants who secure part-time work arrangements (in the case of pregnant or breastfeeding applicants) can also be funded. Furthermore, individual opportunities for further qualification, e.g. conference visits, network exchanges etc., are also eligible for financing. The criteria for receiving a grant are a completed doctorate and an original research topic, which is preferably integrated into the research focus of the Medical Faculty.

This structured program for the scientific and vocational qualification of junior female doctors is named after the Laupheim-born Jewish doctor, Hertha Nathorff (née Einstein), who prior to her emigration to the USA in 1938 had been persecuted by the National Socialists.



Sofia Anastasiadou – Alumni

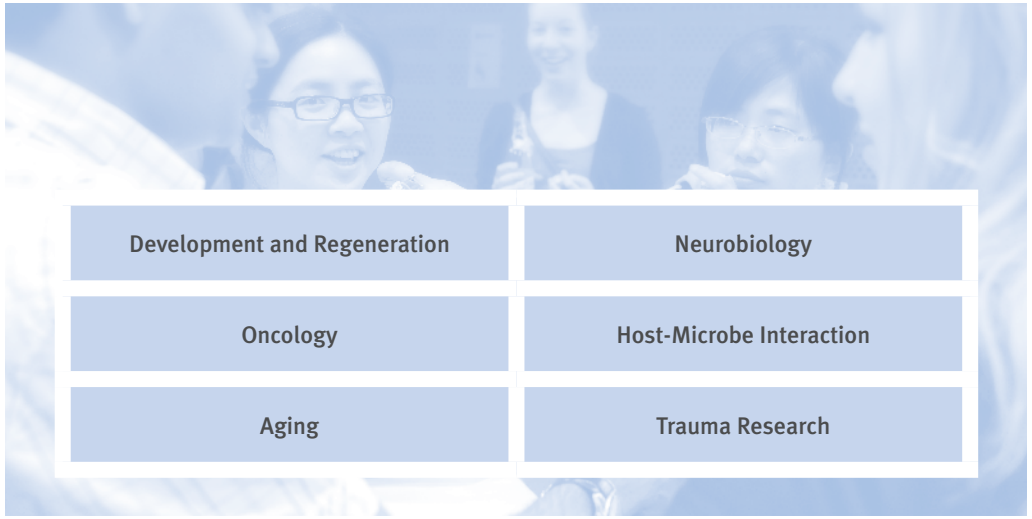
"The Graduate School's PhD program provided me with the optimal conditions to research my PhD thesis. It supported my scientific development by organizing regular progress reports and numerous key competence seminars. Furthermore, the financial support offered by the Graduate School allowed me to attend diverse national and international scientific conferences. Last but not least, the intermediate examinations were a perfect means of motivation to summarize, present and discuss obtained data, and therefore substantially promoted the progress of my PhD project. Taken altogether, the PhD program of the Graduate School provides the ideal conditions for guiding students in the direction of a successful scientific career."

Annemarie Hempel, Dipl.Biol.
"The International Graduate School in Molecular Medicine Ulm provides a unique scientific education beyond the lab bench and allows aspiring researchers to pursue their scientific and academic goals in a congenial and collaborative atmosphere. A multi-member Thesis Advisory Committee (TAC) and frequent evaluations support and promote the students' scientific work throughout their time as a PhD researcher. Furthermore, students benefit exceedingly from the professional training they receive in a variety of key competencies, such as applying for extramural funding or data analysis, which provide them with a variety of skills for the future. Also, interdisciplinary seminars allow students to gain an insight into different research areas and to broaden their horizons. I personally appreciated the generous financial support which allowed me the opportunity to attend international conferences and to discuss my work with renowned experts in my scientific field. The efforts of the IGradU organization team help to strengthen each student's scientific development and I would like to express my deep gratitude for all your excellent work."

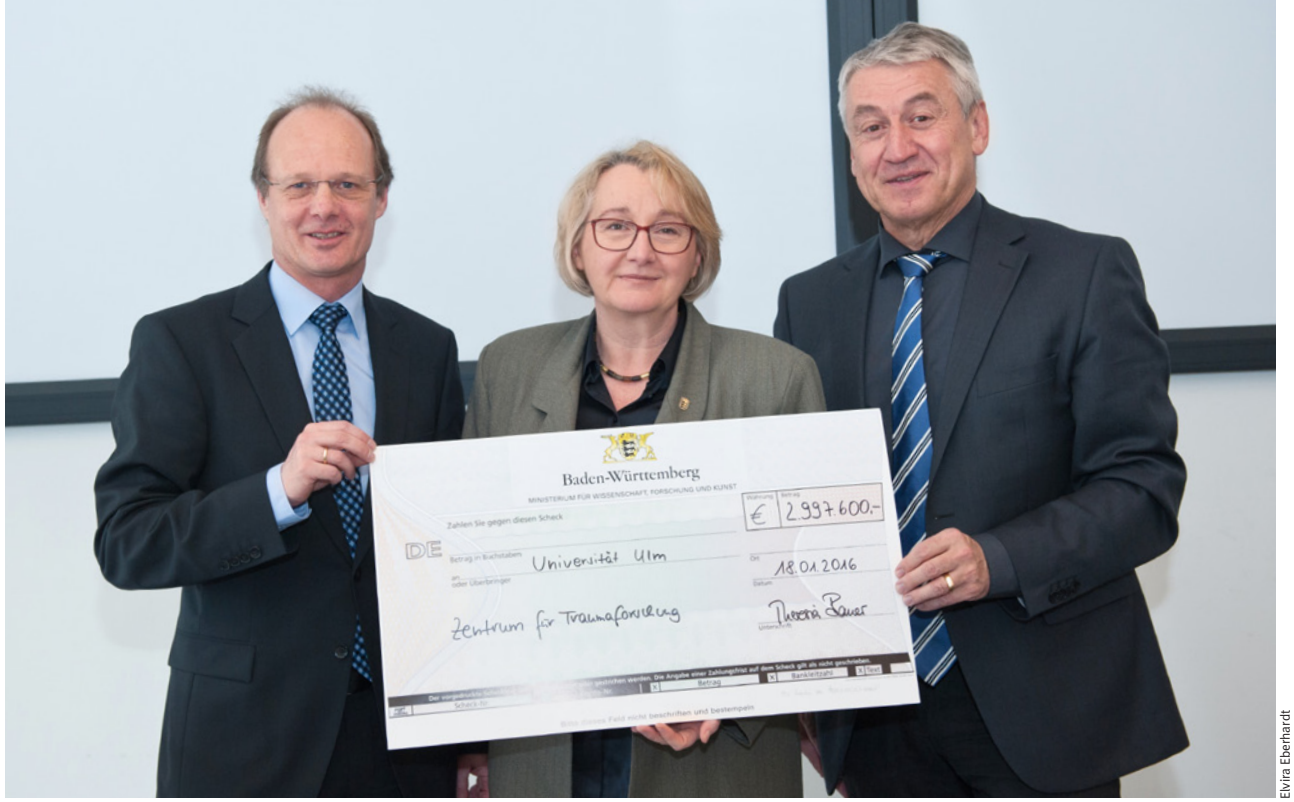
The Graduate School's Research Training Groups

From the beginning of their PhD studies, doctoral students are organized and trained in smaller, thematically focused Research Training Groups in order to concentrate on specific research areas in Molecular Medicine. These Research Training Groups, based on the scientific topics particular to Ulm University, are defined by the Board of the Graduate School and implemented at the International Graduate School in Molecular Medicine Ulm. For each of the six Research Training Groups, one or two persons are responsible for organizing retreats, seminars and activities within their respective Training Group.

The six Research Training Groups are:



The sixth Research Training Group, Trauma Research, has been established due to the successful acquisition of the DFG grant, Collaborative Research Center 1149 – Danger Response, Disturbance Factors and Regenerative Potential after Acute Trauma, and the founding of the Transdisciplinary Trauma Research Center at Ulm University in December 2015. The Transdisciplinary Trauma Research



Elvira Eberhardt

The President of Ulm University, Prof. Michael Weber, and the Dean of the Medical Faculty, Prof. Thomas Wirth, obtain the grant for the Center of Trauma Research from Theresia Bauer, the Minister of Science, Research and the Arts of the state of Baden-Württemberg

Center is supported by the state of Baden-Württemberg with a grant of €3 million over a period of six years. The Medical Faculty of Ulm University co-finances the center with an equal amount of money.

Graduates are actively integrated into the international scientific community. For instance, each year the Graduate School organizes two international meetings where students deliver poster presentations and talks while at the same time having the opportunity to seek advice for their work from professional international scientists. We also hold scientific retreats that are organized either by the students themselves or by principle investigators of IGradU where graduates can exchange ideas among themselves and with senior scientists within a relaxed atmosphere. Furthermore, our PhD students have the chance to attend meetings and conferences abroad with the financial support of travel grants from the Graduate School.

In order to prepare our doctoral candidates for the job market, we offer a large number of key competence seminars in such subjects as project management, bioethics, patent law and copyright law. In addition, we regularly organize career workshops and excursions to pharmaceutical companies.

Alumni

The Graduate School's alumni reflect the excellent education and training of its students. Our alumni are part of a broad and diverse network that includes students from all disciplines and from all over the world.

Our alumni are invited to attend science meetings and seminars organized by the Graduate School. It has always been our aim to bring together former and current students in order to promote an enthusiastic doctoral culture at the Graduate School. To achieve this, we invited our alumni to the "Alumni Homecoming" of Ulm University on 18 July 2015. An interesting program with different activities was presented and there was plenty of time to meet and chat with old colleagues and new students.

Careers

Our alumni work in a variety of sectors. Below is a sample list of places where our former students continue their scientific career:

- Baltech AG, Hallbergmoos/Munich
- Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany
- Cleveland Clinic, Department of Pathobiology, Cleveland, Ohio, USA
- Deutsches Krebsforschungszentrum DKFZ, Heidelberg, Germany
- ETH Zürich, Institut für Pharmazeutische Wissenschaften, Zürich, Switzerland
- French Institute of Health and Medical Research, Saint Augustin, Paris, France
- Fritz-Lippmann-Institut Jena, Germany
- Harvard Medical School, Immune Disease Institute and Children's Hospital Boston, Boston, USA
- Harvard Medical School, Regenerative Medicine Section of Harvard Stem Cell Institute, Boston, USA
- HiPP GmbH & Co. Vertrieb KG, Pfaffenhofen (Ilm)
- Johns Hopkins University School of Medicine, Baltimore, USA
- Max-Planck-Institute, Cologne, Germany
- McGill University, Department of Biochemistry, Montreal, Quebec, Canada
- Medical University of Innsbruck, Division of Clinical Genetics, Austria
- Roche Deutschland Holding GmbH, Penzberg, Germany
- Stanford University School of Medicine, Psychiatry & Behavioral Science, Stanford, USA
- Stanford University School of Medicine, Department of Biochemistry, Stanford, USA
- University of Liège, Coma Science Group, Cyclotron Research Centre, Liège, Belgium
- University of Lund, Lund Center for Stem Cell Biology and Cell Therapy, Lund, Sweden

Our free services include:

- Invitation to events at the Graduate School and Ulm University
- Use of the Career Service of Ulm University – free of charge for graduates up to two years after the completion of their studies
- Alumni email address for life

The Graduate School's Gender Equality Programs

At present, 68% of our doctoral candidates are female. Special initiatives have been established for the benefit of female doctoral students, single parent doctoral students, doctoral students with children, and doctoral students during pregnancy.

Childcare Programs

In order to enable PhD students with children to pursue their work, the Graduate School offers various childcare programs. Our childcare programs provide financial support for childcare during meetings and conferences, stays abroad and for childcare services outside the regular business hours of daycare centers. We can also offer practical help in finding the right daycare center.

Technical Assistance

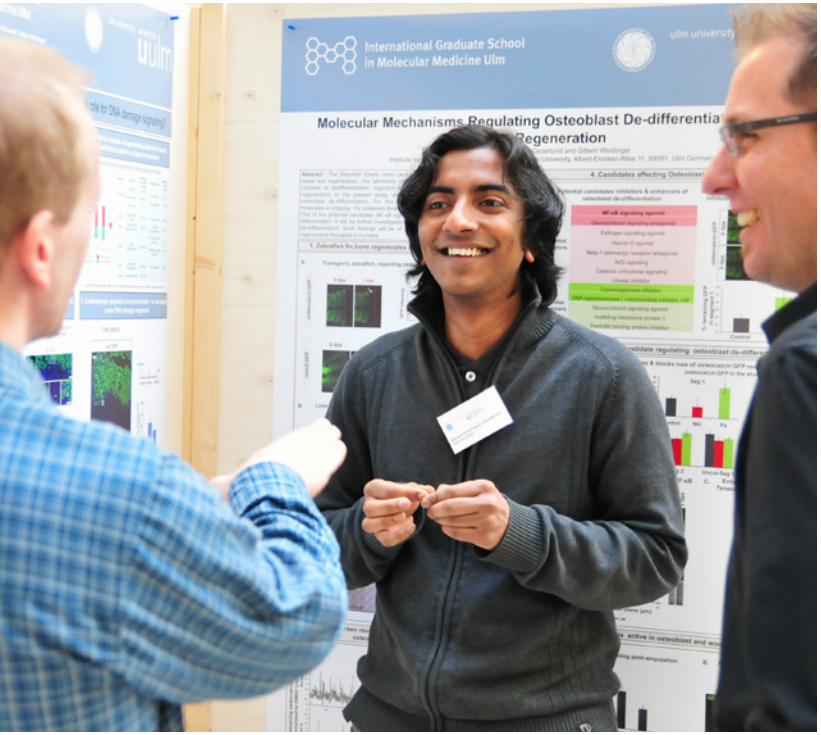
The Graduate School finances the employment of technical assistants to conduct experiments for students during pregnancy and maternity leave as regulated by law. This enables female students to continue their PhD work during and after pregnancy without the loss of precious time. This financing of technical assistants by the Graduate School is possible for a maximum period of one year.

Female Mentoring

A Mentoring and Training program (*MuT*) enables our highly qualified female scientists to become acquainted with the ways and means of successfully tapping their career potential and exploring the opportunities available to them. It is there to support their personal development and assist in planning their careers.

Scholarships

Many institutions offer a variety of scholarships for female students and those with children. The Graduate School provides information regarding the possibilities of financial support and assists students in receiving these scholarships in order to alleviate the conflicting demands of studying and family life.



The Graduate School's Mentoring Programs

Scientific Mentoring

The training of outstanding researchers is the key task of the International Graduate School in Molecular Medicine Ulm. As mentioned before, our major aims in this respect are:

- Cutting-edge research training of junior scientists
- Scientific independence and the self-responsibility of PhD students
- Improvement of employability through training in key competencies

Each doctoral student is supervised by an interdisciplinary and international Thesis Advisory Committee (TAC) which is involved in ensuring interdisciplinary training and mentoring in research. Each TAC consists of three members:

- The group leader of the laboratory where the thesis work is performed
- A scientist from another institute of Ulm University
- An external reviewer, either from industry or from a research institute

Furthermore, a member of the School's Junior Faculty (see pages 13 and 155) can be integrated into the TAC as an additional member.

The TAC supervises PhD students in their daily laboratory work to help them with formal or technical problems, and to evaluate oral examinations and their written dissertation. This multiple supervision approach supports the independence of our PhD students as junior researchers.

Social Mentoring

Apart from their scientific training, our doctoral students are offered mentoring on different levels to facilitate their stay in Ulm in order to integrate them into German society and the scientific community, and to help them concentrate fully on their academic performance in their chosen field of scientific research.

Our Coordination Office assists graduates with the organization of their studies within the *International PhD Programme in Molecular Medicine*, and of their study life in general. This office is the first point of contact and assists applicants even before their first acceptance into the program as well as throughout the period of their PhD studies up to their final graduation. It also advises on issues concerning visas, contracts, work permits, accommodation, and health insurance etc. At the beginning of every semester, the Coordination Office holds an introductory session where all necessary information is given about the program, the duties required and what is offered.

Each year the graduates elect three students to represent their interests on the various boards and committees of the Graduate School and to act as their official contact concerning student issues.

M4M (Mentorship for Molecular Medicine) is a social mentoring program that brings together doctoral students and senior members of the community living in Ulm for mutual exchange and support. The idea behind the program is to give our international students a positive impression of everyday German culture through a variety of social activities, such as excursions, intercultural workshops and themed evenings. This personal contact and individual support gives students the opportunity to participate more easily in German society.

Senior consultants support doctoral students even before their arrival in Ulm and help them to find their way during their first days and weeks in a new country. Regular meetings and personal contacts between PhD students and senior consultants help to develop an atmosphere of confidence and familiarity.

Mentorship for Molecular Medicine PhD Students

Female Mentoring

The Graduate School supports the participation of junior female academics in the MuT-Program (Mentoring and Training Program). MuT enables highly qualified female scientists to become acquainted with the ways and means of successfully tapping their career potential and of exploring the opportunities available to them. It supports their personal development and assists in planning their careers.

Barbara Eichner

Activities of the Graduate School

Excursions
Getting in touch with future employers:

One of our main objectives is to bring doctoral students into contact with potential industrial employers. For this reason, we regularly organize excursions to pharmaceutical and biotech companies. At these events, our students not only receive information about the working field of each company but also gain a deeper insight into the career opportunities available to highly qualified PhD graduates.

Every year there are at least three excursions organized by the Graduate School. So far, we have visited:

- Amgen Research, Munich
- Atlas Pharma, Konstanz
- Boehringer Ingelheim, Biberach an der Riss
- CANDOR Biosciene, Weißensberg
- Carl Zeiss AG, Oberkochen
- Sanofi-Aventis, Berlin
- Rentschler Biotechnologie GmbH, Laupheim
- Roche, Penzberg

The Graduate School's Key Competence Training Program

Members of the Graduate School are supported by a wide range of additional seminars and workshops. Our training program in key competencies is designed to equip doctoral students with a full range of skills which will improve their effectiveness as researchers and ensure that they are not only highly qualified but employable in a variety of careers by the end of their studies.
Our training program has been created especially for our students and is customized to deal with those situations and problems that can arise while engaging in doctoral research. We work with highly qualified trainers and experts who have usually worked in the academic field themselves and have at hand a wealth of practical experience.

The Graduate School's key competence courses are open to all members of the Graduate School. No fees are charged for attending our courses. All courses are held in English or German. We offer courses in project management in biotech industries, (extramural) funding, scientific writing and presentation skills, good manufacturing practice, bioethics, copyright law, patent law, and career workshops often on a biannual basis.

Retreats

Every year we organize at least one retreat and mini symposia focusing on certain research fields pursued at our Graduate School. At these events, our PhD students can exchange ideas with each other and obtain advice on specialized topics from senior scientists in a relaxed and natural environment outside Ulm. Moreover, the retreats are a great opportunity to get to know each other away from work and to relax in a pleasant atmosphere. Some retreats are held together with our international partner institutions. Among these locations, we have so far been to Switzerland, Scotland, USA, Greece, Italy and Finland.

In addition to our Gender and Mentoring Programs, we offer a variety of complementary benefits for students

Our program offers a large number of benefits for students. The most frequently requested programs include:

Mobility Program

In order to enhance the integration of our students into the international scientific community, the Graduate School offers a mobility program awarding financial support to students wishing to participate in meetings and engage in practical training. Students can obtain funding for short visits to national and international conferences and for long-term stays and internships at laboratories lasting up to several months.

Joint Degree Programs

The International PhD Programme in Molecular Medicine has established joint PhD programs with the University of Padua, Italy, and the University of Oulu, Finland. To obtain a joint degree, candidates must stay for at least six months at the host university and, depending on which of these universities is chosen, one of the TAC members must be from either Padua or Oulu. The establishment of such joint degree programs is part of the internationalization strategy of IGradU. All costs related to the exchange programs are covered by the Graduate School.

Doctoral Student Award

To motivate doctoral students and to honor extraordinary achievements, the Doctoral Student Award is presented once a year by the Graduate School. Awards are conferred for exceptional research, as documented in publications or as talks given at international scientific conferences, and for the development and implementation of innovative novel methods. Interdisciplinary projects are given preferential consideration. Students are free to use this award for any purpose that helps to promote their career in the field of science.

Postdoc Fellowships and Programs

The Graduate School provides postdoctoral fellowships for a period up to six months for outstanding doctoral students planning to apply for a postdoctoral academic position abroad. This is an important benefit since applications for postdoctoral fellowships are normally evaluated over a period of up to six months. Key competence courses also offer assistance in writing grant applications and have proved useful for those beginning a new postdoctoral career.

Social Activities

The Graduate School organizes regular social activities, for example, Christmas and summer parties (often with sports activities such as bowling or mini golf) to create a friendly atmosphere and foster a team spirit between doctoral students and supervisors. We offer excursions to the Oktoberfest and, with our partner M4M we visited Neuschwanstein Castle, Basel, Nürnberg and we will visit Berlin in 2016. Each year many PhD students and their supervisors take part in the biggest marathon in Ulm known as the “Einstein-Marathon.” In addition, our student representatives organize a regular “Stammtisch” (“get-together”) and other smaller events.

The IGradU team took part in the biggest marathon in Ulm, known as the “Einstein-Marathon”

The Graduate School's International Networking

Scientific excellence not only depends on the outstanding performance of talented young researchers but also on the close cooperation with a worldwide network of renowned partner institutions. Consequently, the Graduate School is making strong efforts to develop a doctoral training program within an international context. A central element of our internationalization strategy is the promotion of international cooperation in the form of exchange programs, summer schools and international PhD programs. Since its foundation in 2006, the Graduate School has cooperated closely with, among others, the following international partner institutions:

- Johns Hopkins University School of Medicine, Baltimore, USA
- Houazhong University of Science and Technology/Tongji Medical College in Wuhan, China
- University of North Carolina at Chapel Hill, USA
- Southeast University (SEU), Medical School, Nanjing, China
- Center for Stem Cell Biology and Regenerative Medicine, University of Tokyo, Tokyo, Japan

Moreover, together with the partner institutions in Oulu, Finland, and in Padua, Italy, the Graduate School offers the possibility of obtaining a double-degree.

1. TissueHome: Joint PhD program in cooperation with the Biocenter Oulu, Finland

Tissue homeostasis describes the property of organs and tissues to maintain their functional capacity during development, adulthood and aging. This includes the ability of tissue turnover under normal conditions, the ability to regenerate lost tissue upon injury, and the possibility to compensate a loss of organ function by other means. There is increasing evidence that the capacity of stem cells as well as somatic cells contribute to tissue homeostasis and that organ regeneration decreases during the life cycle (embryogenesis, adulthood and aging). Thus, understanding the regenerative capacity of somatic cells and stem cells is a key question in our aim to improve healthy aging.
The TissueHome consortium, consisting of scientists from the Biocenter Oulu, University of Oulu and the Medical Faculty of Ulm University, therefore aims to understand in more detail properties contributing to tissue homeostasis and thereby will train the next generation of scientists in an interdisciplinary and international context to be able to obtain a comprehensive view of key processes of homeostasis and their changes in aging, and how we can establish novel avenues for therapies.

Currently, a total of ten doctoral students are participating in the joint-degree program.

Administration of the program
The TissueHome students are affiliated to the Graduate School and the doctoral program of their home university, and follow the study curriculum of their home institution. Each partner has a joint PhD program coordinator at their institution.

Student admission requirements and processes
The TissueHome Steering Committee selects and accepts the students into the joint degree program. A home university is appointed individually for each student and this is where the Principal Supervisor is based. Before students can officially start on the program, they must have doctoral study rights at their home university. During the time of exchange (at least six months in total), each PhD student should also be enrolled at the guest university in an appropriate manner.

Supervision and follow-up
Each student has at least two supervisors, which includes at least one from each university. One supervisor in the home university is nominated as the Principal Supervisor. The supervisors undertake to provide advice for the doctoral candidate and to jointly direct the research program. A Supervision Agreement will be issued individually for each PhD student enrolled and will be signed by the PhD student, a legal representative of the University of Oulu, the Chairman of IGradU, and one supervisor from each participating university. Moreover, an annual rotating retreat, at which both doctoral students and their supervisors meet, will take place either in Finland or in Germany.

2. Double Degree PhD Program in cooperation with the University of Padua (Italy)

Doctoral students taking part in this Double Degree PhD Program are supervised by Thesis Advisory Committees consisting of scientists from Ulm and Padua. The exchange time lasts at least six months to achieve a double diploma that is recognized by both universities.

The Double Degree PhD Program between the IGradU (Ulm University) and *Scuola di Dottorato in Bioscienze e Biotecnologie, Università degli Studi di Padova* (University of Padua, Italy) was launched in 2009 and has been running successfully since that time. Two of our doctoral students have already obtained this double degree with a further three students to follow.

Regulations for Ulm-based students:
The PhD-students are required to spend at least six months (not necessarily uninterrupted) at the host university (*Università degli Studi di Padova*). The thesis will be submitted and discussed in English. The doctoral studies will end with one final examination to be held at Ulm University.
Currently, both the joint PhD programs with Oulu and with Padua, are expanded on the master's level. It is planned that the joint master's program in Molecular Medicine with Padua will start in the winter term of 2016/2017, and the joint master's program with Oulu in the winter term of 2017/2018.

Nanjing

A delegation from the Medical Faculty of Ulm University and IGradU visited the Medical School of Southeast University in Nanjing in May 2013. The aim was to establish a scientific exchange program. This program began in September 2013 when the first Chinese students started their practical work in the laboratories of Ulm University.

Chapel Hill

The Graduate School has a partnership with the University of North Carolina at Chapel Hill, USA. PhD students from Ulm undertake joint scientific projects between Ulm and Chapel Hill, and complete a part of their studies at Chapel Hill.

Wuhan

Each year the Graduate School organizes summer schools abroad with the ultimate goal of presenting Ulm-based research in order to increase the international visibility of the school and to recruit highly qualified PhD candidates. The first Summer School to be held at Houazhong University of Science and Technology/Tongji Medical College in Wuhan, China, took place in August 2007. The chosen topic of the tenth Summer School in Wuhan in 2016 is *Oncology*.
In June 2013, a new cooperation contract between Ulm University and Tongji Medical College was signed. The aim is to further strengthen the scientific cooperation between scientists and students, especially in combination with the International Graduate School.

Guest Professor, Guest Scientist and Guest Speaker Programs

The International Graduate School in Molecular Medicine has three programs that aim to strengthen and improve international cooperation, sharpen the internationalization strategy of the Graduate School and expand the teaching offer to our students.

Long Term Guest Professor Program
The first program (*Gastprofessorenprogramm des Landes Baden-Württemberg*) is funded with €50,000 by the state of Baden-Württemberg and aims to bring renowned, top-class experts to Ulm. IGradU supports this program with the same amount of money. The Guest Professor is expected to visit Ulm several times per year and to contribute to research and teaching at the Graduate School. After Prof. Hiromitsu Nakauchi from Tokyo, Prof. Philip Wong from the Johns Hopkins University School of Medicine, Baltimore, took on the guest professorship in 2014. Prof. Wong works on animal models of neurodegenerative diseases and established a research group with one of our alumni in the same research field.

Short Term Guest Professor/Guest Scientist Program
The second program is a Guest Scientist/Guest Professor Program that allows collaborating partners to visit Ulm for a period of ten to fourteen days to strengthen cooperation, to work in the labs and to give talks/courses for our students.

Here are some examples from the last two years:

- Bénédicte Chazaud, Centre de Génétique et de Physiologie Moléculaire et Cellulaire, University of Lyon, France
- Vanesa Gottifredi, Cell Cycle and Genomic Stability Laboratory, Instituto Leloir Fundación, Buenos Aires, Argentina
- Thomas Kitzmann, Biochemistry and Molecular Medicine, University of Oulu, Finland
- Rhett Kovall, Biochemistry and Microbiology, College of Medicine, Department of Molecular Genetics, University of Cincinnati, USA
- Elizabeth Mellins, Division of Pediatric Immunology and Transplantation Medicine, Stanford University, USA
- Eduardo Perozo, Department of Biochemistry and Molecular Biology and Institute for Biophysical Dynamics, University of Chicago, USA
- Lorenzo Pinna, Venetian Institute for Molecular Medicine, Padua, Italy
- John Sinclair, Molecular Virology, School of Clinical Medicine, University of Cambridge, UK
- Robert Tarran, Department of Cell Biology and Physiology, University of North Carolina at Chapel Hill, USA
- Per Westermark, Department of Immunology, Genetics and Pathology, Uppsala University, Sweden

Guest Speaker Program
The third program is a Guest Speaker Program that brings collaboration partners to come to Ulm to present and discuss their results with our scientists. The visits are limited to one to two days. This program is also meant to encourage our students to actively invite scientists of interest to visit Ulm University.

The Graduate School currently collaborates with 30 institutes and 15 medical departments of Ulm University.

Institutes of Ulm University

Central Institution of Electron Microscopy
Division of Neurophysiology
Institute of Analytical and Bioanalytical Chemistry
Institute for Anatomy and Cell Biology
Institute of Applied Biotechnology, Biberach
Institute of Applied Physiology
Institute of Biochemistry and Molecular Biology
Institute of Biophysics
Institute of Clinical and Biological Psychology
Institute for Clinical Transfusion Medicine and Immunogenetics Ulm
Institute of Experimental Cancer Research
Institute of Experimental Physics
Institute of Forensic Medicine
Institute of General Physiology
Institute of Human Genetics
Institute of Medical Microbiology and Hygiene
Institute of Microbiology and Biotechnology
Institute of Molecular and Cellular Anatomy
Institute of Molecular Endocrinology of Animals
Institute of Molecular Genetics and Cell Biology
Institute of Molecular Medicine (ZIBMT)
Institute of Molecular Virology
Institute for Medical Systems Biology
Institute of Organic Chemistry III
Institute of Orthopedic Research and Biomechanics
Institute of Pathology
Institute of Pharmacology of Natural Products and Clinical Pharmacology
Institute of Pharmacology and Toxicology
Institute of Physiological Chemistry
Institute of Virology

Medical Departments

Center of Internal Medicine
Department of Internal Medicine I
Department of Internal Medicine II
Department of Internal Medicine III

Surgery Center
Orthopedics Clinic
Psychosomatic Medicine and Psychotherapy Clinic
Department of Anesthesiology
Department of Child and Adolescent Psychiatry/Psychotherapy
Department of Dermatology and Allergic Diseases
Department of Gene Therapy
Department of General and Visceral Surgery
Department of Gynecology and Obstetrics
Department of Neurology
Department of Orthopedic Trauma, Hand, Plastic and Reconstruction Surgery
Department of Otorhinolaryngology (HNO)
Department of Pediatrics and Adolescent Medicine

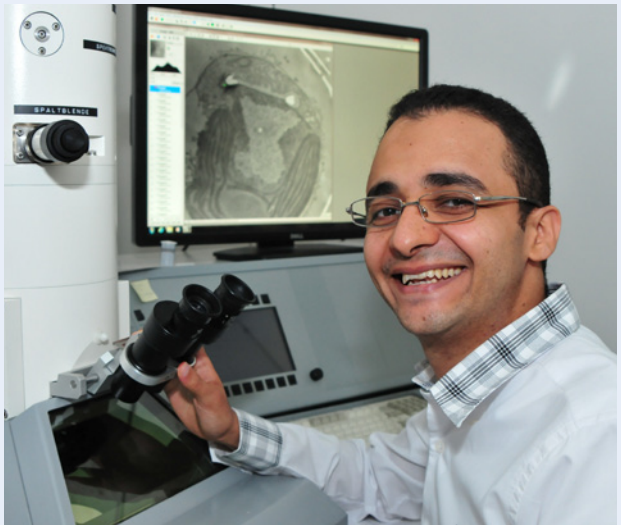
Junior Faculty

Department of Internal Medicine III
Institute for Anatomy and Cell Biology
Institute of Applied Physiology
Institute of Biochemistry and Molecular Biology
Institute of Immunology
Institute of Pharmacology of Natural Products & Clinical Pharmacology
Institute of Virology

On the following pages, we present the research projects of the doctoral students and the Junior Faculty members of IGradU.

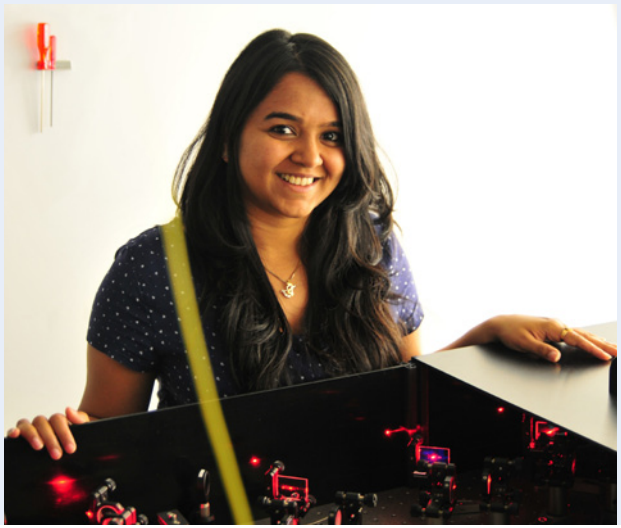
Elvira Eberhardt

Our Doctoral Students



Mohamed Essam Ahmed Abdellatif

Born in 1983, I was awarded a BSc in Microbiology and Chemistry from Ain Shams University (Egypt) and a MSc in Biology from Ulm University (Germany). My main research interest involves addressing biological processes utilizing advanced electron microscopy at the Central Facility for Electron Microscopy, Ulm University. I have been at IGradU since the winter semester of 2014.



Harsha Agarwal

Born in 1990, India, I did my under-graduation in Amity University (India) in B.Tech Biotechnology. Further I did my MSc in Advanced Materials in Ulm University (Germany). I am pursuing my PhD at the Institute of Biophysics, Ulm, under the supervision of Prof. Dr. Christof Gebhardt and am also engaged in research at the International Graduate School in Molecular Medicine, Ulm. This is my first year in the program.

Correlative 3D imaging at macromolecular resolution, combining fluorescent microscopy, FIB-SEM and STEM-tomography, promises new insights into HCMV infection and nuclear actin organization

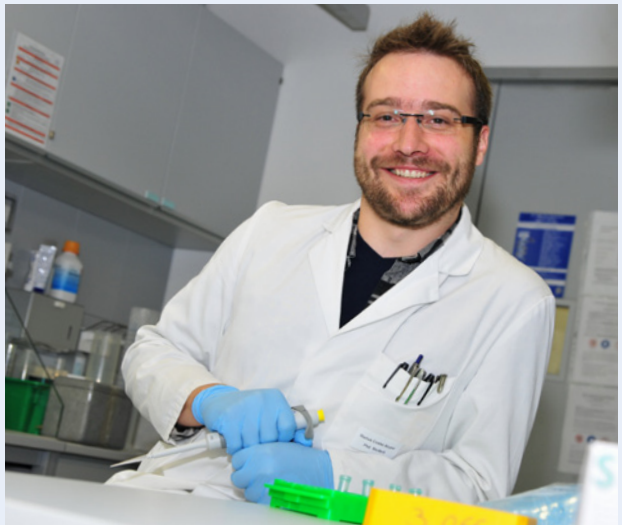
The project addresses two main biological processes utilizing advanced techniques in electron microscopy. Firstly, the entry process of the HCMV (human cytomegalovirus) into fibroblasts and endothelial cells. It is assumed that HCMV entry into fibroblasts takes place by fusion with the plasma membrane. Meanwhile, its entry into epithelial and endothelial cells involves a macropinocytosis-like pathway at the plasma membrane followed by fusion with an endosome. Secondly, the structure and distribution of the endogenously expressed nuclear actin filaments in mammalian cells (fibroblasts and primary neurons). The studies that supported the nuclear actin existence triggered a strong debate and were unconvincing for some. Currently, only a few studies have managed to address the structure and distribution of the nuclear actin filaments. The techniques utilized, as far as the instrumentation and sample preparation are concerned, challenge the limitations posed by classical biological electron microscopy (e.g. classical 2D images and the artefacts imposed on biological specimens via fixation). Furthermore, fluorescence and electron microscopy approaches are utilized in a form of a CLEM (correlative light and electron microscopy) using fluorescent tags (e.g. GFP) via molecular cloning techniques to better address the above-mentioned biological processes.

Single molecule and superresolution microscopy in mammalian cells

My field of research revolves around localizing the protein CTCF (11-zinc finger protein or CCCTC binding protein), which is said to have transcriptional functions, in a mammalian cell line using single molecule and superresolution microscopy. The aim is to know how these proteins are organized at the nanoscale level as this will further help in knowing more about its biological functions.

Single molecule methods, such as Stochastic Optical Reconstruction Microscopy (STORM), provide resolutions down to a few tens of nanometers by the cycling of dyes between its fluorescent and non-fluorescent phase, and hence have revolutionized fluorescence microscopy. It provides a versatile method to achieve a higher resolution than a light microscope. There are various pre-imaging techniques required, such as labeling of secondary antibodies with dyes and then immunostaining the fixed cells in the optimized way possible to attain good signal to noise ratio. Also, the buffer conditions for STORM measurements should be optimized to obtain a useful reconstruction and localization. Therefore, my goal will be to attain the optimum conditions for a better understanding of the distribution of CTCF.

In addition, I am constructing plasmids with the gene of interest (CTCF wild type and mutated forms) using Gateway cloning systems and also introducing tags such as Halo so as to measure its kinetics in STORM (using various dyes). Overall, this is an interesting blend of studying the localization precision of proteins using the optics principles in a STORM setup.

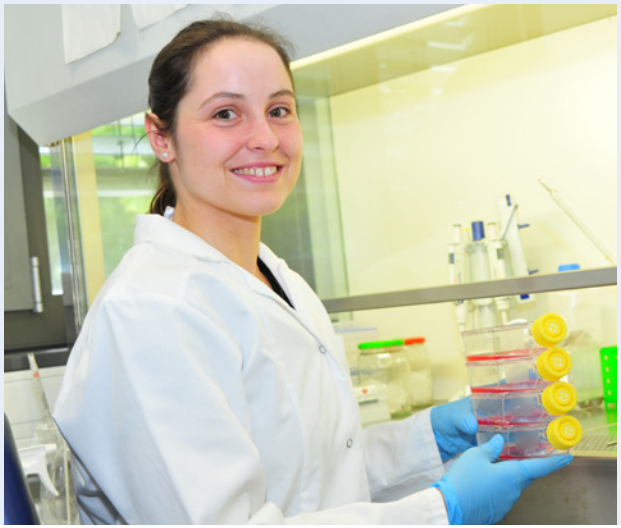


Marius-Costel Alupei

I was born in Romania in 1988 in a part of the country also known as Buchenland. I completed my studies in Cluj-Napoca (Klausenburg) and started my PhD at Ulm in 2014 in the Department of Dermatology and Allergic Diseases in the CEMMA (Cellular and Molecular Mechanisms in Aging) program.

Loss of proteostasis as the pathomechanism in a premature aging disease

Cockayne Syndrome (CS) is a premature aging disease, a genetic condition that can be caused by mutations in five different genes encoding for DNA-repair proteins (CSA, CSB, XPB, XPD, and XPG). CS is characterized by neurological degeneration, cataracts, alopecia and severe growth failure ("kachectic dwarfs") with a median life expectancy of 12 years. It is already known that complete failure of DNA repair does not necessarily lead to premature aging and developmental delay, and thus an alternative function of the CS proteins might account for the disease. The main characteristic of CS cells is the failure to recover RNA synthesis after UV irradiation, a feature shared with cells from UV-sensitive syndrome (UVsS) and a mild UV-sensitive skin disorder that can be also caused by mutations in CSA or CSB. Therefore, the failure to recover RNA synthesis after UV irradiation cannot be responsible for developmental delay and premature aging. In my project, I study the implication of CS proteins in other cellular processes, such as Pol I transcription and ribosomal biogenesis. A malfunction of these processes can cause a reduction of the total amount of ribosomes in the cells, as well as the incorrect translation of proteins. Zooming inside the endoplasmic reticulum (ER) – the cellular compartment where posttranslational modifications take place – could provide answers regarding the ER stress status of CS cells and a way of improving protein translation by reducing and controlling the ER stress.



Eva Barth

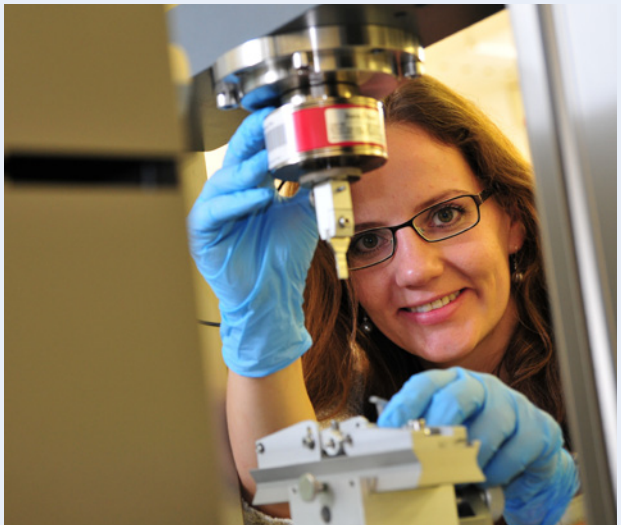
Born in 1988. After her bachelor's in Molecular Medicine at Ulm University, Eva gained her master's in Molecular Biosciences at the University of Heidelberg. In 2013, she started her PhD at the IGradU in the research training group known as CEMMA (Cellular and Molecular Mechanisms in Aging) at the Institute of Experimental Neurology under the supervision of PD Dr. Anke Witting and Dr. Katrin Lindenberg.

Age-related mitochondrial and metabolic dysfunction in HD and ALS

Mitochondrial abnormalities and aging belong to the primary risk factors of neurodegenerative diseases such as Huntington's disease (HD) and amyotrophic lateral sclerosis (ALS). Involvement of mitochondria in HD and ALS is further supported by the characteristic weight loss of patients suggesting a dysregulation of energy metabolism. Therefore, we focus on the mechanisms underlying age-related mitochondrial changes in HD and ALS.
Members of the protein family of sirtuins are known for their anti-aging effects. For human longevity, Sirt3 seems to be important. Sirt3 activity depends on NAD+ and it is located in mitochondria deacetylating proteins which regulate ROS defense and energy metabolism. Furthermore, Sirt3 reduced fragmentation of mitochondria in an ALS model of cultured cortical neurons. Considering these facts we examine the role of Sirt3 during the course of disease in a mouse model of HD (R6/2) and ALS (SOD1G93A). The brain and spinal cord of the mice, as well as cultured primary brain cells, are investigated according to Sirt3 levels. Cell culture experiments are valuable for cell type-specific stimulation and response analysis. Microglia cells are especially interesting due to their role in inflammatory processes, where Sirt3 is involved as well. For determination of Sirt3 activity, we immunoprecipitate target proteins of Sirt3 and determine their acetylation status subsequently by Western Blot.
In summary, we examine the role of Sirt3 related to mitochondrial and inflammatory age-related changes in HD and ALS.

Richard Bauer

Born in 1989, Richard has been employed since the winter semester of 2014/15 at the Institute of Medical Microbiology and Hygiene in the working group of Prof. Dr. Spellerberg. The group focuses on molecular mechanisms of streptococcal pathogenicity. One of the main goals of the group is the identification and characterization of virulence determinants that counteract innate immunity mechanisms of the human host.



Stephanie Baur

Born in 1986. After studying biology, she started her PhD at the Institute of Orthopedic Research and Biomechanics in a project funded by the German Research Foundation, and then joined the IGradU in April 2013. She is interested in the effects of the immune system on regular fracture healing and on fracture healing influenced by a posttraumatic systemic inflammation.

Virulence regulation in *Streptococcus anginosus*

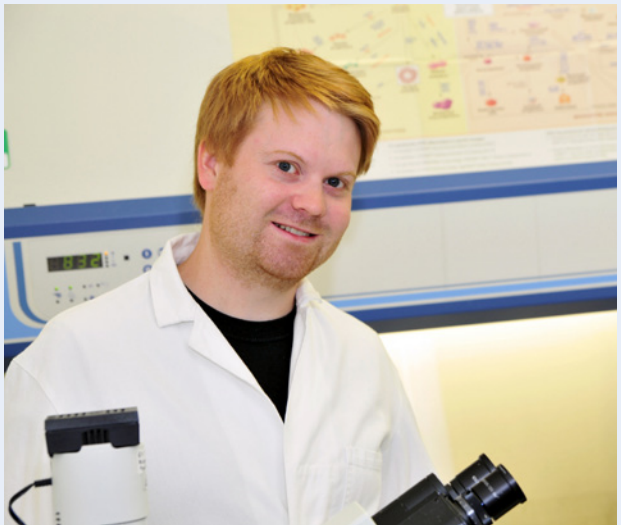
Streptococcus anginosus is one of three members of the correspondent *Streptococcus anginosus* group (SAG). Bacteria of this group are usually considered as commensals of mucosal membranes. However, they possess an underestimated pathogenic potential which is reflected in the high incidence rate caused by SAG bacteria among invasive streptococcal infections. SAG members are frequently isolated from abscesses and blood samples of sepsis patients. Additionally, they are reported as emerging pathogens in cystic fibrosis patients. Despite their important clinical role, the factors involved in the colonization and invasion of their host are largely unknown.
One exception is the β-hemolysin which was identified by our group. However, regulation mechanisms controlling the expression of the β-hemolysin genes in *S. anginosus* have not been elucidated so far. Therefore, the aim of this PhD project is the identification and characterization of a virulence regulator in *S. anginosus*. On the basis of the hemolysin expression, virulence regulation will be identified and characterized. The function of the identified target genes will be analyzed to gain an improved understanding of virulence mechanisms in *S. anginosus* that could serve as a basis for the development of further treatment strategies.

The role of the C5a complement receptor C5aR in fracture healing after severe trauma

The complement system is part of the innate immune system and crucial for the defense of pathogens and the induction of inflammation, and may also be involved in bone biology. Fractures are the most frequent injuries in patients with multiple traumata. Severe injuries induce systemic inflammation and can lead to impaired fracture healing. It was shown that the complement anaphylatoxin C5a is strongly up-regulated in severely injured patients with posttraumatic inflammation. C5a binds to its receptor C5aR, thereby inducing cell migration and inflammatory responses in immune cells. We demonstrated that C5aR is also expressed by bone cells and regulates osteoblast migration and immune response *in vitro*. However, it remains an open question whether osteoblasts are target cells for activated complement in bone healing *in vivo*.
Therefore, Stephanie analyzed the role of C5aR in fracture healing under regular conditions and after severe trauma. Using mice with an osteoblast-specific overexpression of C5aR and C5aR-knockout mice, she already demonstrated that osteoblasts might be important target cells for C5a because fracture healing in C5aR-tg mice was impaired. Healing was also impaired in C5aR-knockout mice, suggesting that a balanced activation of complement is important for fracture healing under regular and compromised conditions. The current results of this study implicate that pharmacological complement modulation might be beneficial for the treatment of impaired fracture healing in severely injured patients.

Hanna Bayer

Born in 1988, she is currently doing her PhD in the Department of Experimental Neurology in the lab of PD Dr. Anke Witting. In 2012, she started her PhD at the IGradU. Already during her master course, she focused her research on neuroscience.
Besides her studies, she works on the Student Council to improve the course of study in Molecular Medicine.



Alexander Becher

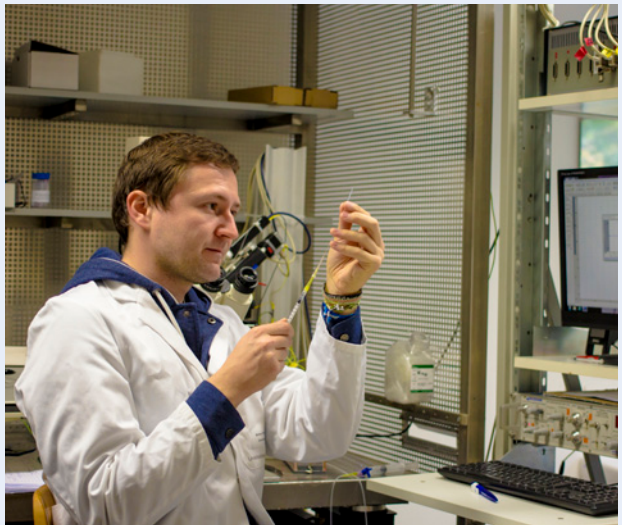
After completing his studies in Technical Biology at the University of Stuttgart, Alex joined the PhD program of the International Graduate School in Molecular Medicine in 2013. He is currently working in Prof. Dr. Seufferlein's research team in the Department of Internal Medicine I and is focusing on the molecular characterization of cellular secretion processes, particularly in cancer cells.

Effect of ALS-related genes on the PGC-1α signaling system

Amyotrophic lateral sclerosis (ALS) is a progressive dysfunction and rapid degeneration of motor neurons in the cerebellar cortex, brain stem and spinal cord, leading to focal muscle wasting and weakness. In addition, patients show also a metabolic phenotype, namely, weight loss, hypermetabolism and hyperlipidemia. This might be related to mitochondrial and metabolic abnormalities that can be detected on a cellular level not only in ALS but also in other neurodegenerative diseases characterized by a metabolic phenotype. The hypothesis of the project is that these metabolic changes might be related to the metabolic master regulator peroxisome proliferator-activated receptor (PPAR) gamma coactivator-1α (PGC-1α), a transcriptional co-activator important for mitochondrial biogenesis and function. Indeed, changes in the PGC-1α-mediated transcription occur in Huntington's disease and Parkinson's disease. Furthermore, we found that a SNP in the brain-specific promoter region of PGC-1α has a male-specific influence on age of onset and age of death in men and rodents. In addition, PGC-1α deficiency has a disease-accelerating effect in an ALS mouse model (Eschbach et al. 2013).

A novel role of the armadillo protein p0071 in cellular secretion

The protein p0071 (also known as plakophilin 4 /PKP4), together with p120 -catenin, NPRAP, ARVCF and plakophilin 1-3, is part of the p120ctn subfamily of armadillo repeat proteins. P0071 has been implicated in various cellular contexts such as intercellular adhesion, neurite outgrowth, cytoskeletal organization and cell division via controlling Rho-GTPase signaling. In a yeast-two-hybrid Screen for protein-protein interactions performed by the group of Prof. M. Hatzfeld, a total of 171 potential interaction partners for p0071 were identified that included proteins with vital functions in cell adhesion as well as cytoskeleton-associated proteins. Interestingly, around 25% per cent of the identified proteins were commonly assigned to cellular transport processes and/ or bind to transport vesicles. A potential role of p0071 in transport and secretion seems therefore likely but has not been reported in any literature so far. Among the already described interaction partners, kinesin-like motor protein KIF3B belongs to a microtubule-based transport complex and directly binds p007. Deregulated secretion is a hallmark of various cancer subtypes. Our goal is thus to identify and characterize functions of p0071 within the cellular transport machinery and to examine in particular whether p0071 is essential for effective transport of substrate proteins of the KIF3 complex.



priv.

Marcin Bednarz

Born in 1984 in Rzeszów, Poland, he went to school in Germany and finished his master's degree in 2011 at the Justus-Liebig University in Giessen. Shortly afterwards in 2012, he started his PhD thesis in the Division of Neurophysiology at Ulm University and joined the Graduate School in Molecular Medicine in the summer semester of 2012.

Alberto Bertozzi

I was born in 1987. I joined the International Graduate School in Molecular Medicine in October 2014. I work in the group of Gilbert Weidinger at the Institute of Biochemistry and Molecular Biology. The topic of my PhD is heart regeneration in zebrafish and my project focuses on the role of the transcription factor Sox9 during the regeneration process.

Pathogenesis of neuromuscular diseases

Mutations in genetic coding for ion channels can lead to diseases known as "hereditary channelopathies." Episodic attacks of coordination disorders, loss of muscle strength, cardiac arrhythmia, and anesthesia-related events are characteristic of channelopathies. Like all muscle diseases, muscle channelopathies are rare diseases.

We express disease-causing mutated and control wild-type channels in standard cell models, such as human embryonic kidney cells (HEK, tsA201), skeletal muscle cells (c2c12, GLT) or *Xenopus laevis* oocytes.

With electrophysiological methods, such as the cut-open or the patch-clamp technique, we can observe ion movement through these expressed channels as an ampere current appearing at different controlled voltage values that allows us to describe the functional properties of these ion channels. Changes between mutated and wild-type channels are analyzed and compared to the patient's phenotype carrying the mutation in order to find a possible explanation for the disease. The investigating focus here lies mainly in voltage-gated sodium and calcium channels.

This work compares individual approaches in connecting electrophysiological data to neuromuscular diseases showing novel mutations and their pathogenic explanations.

The role of the transcription factor Sox9a in zebrafish heart regeneration

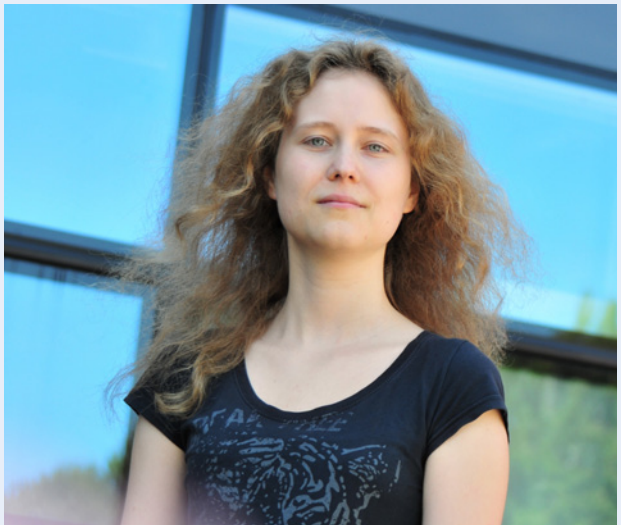
In humans, ischemic damage to the heart is a leading cause of death since it results in permanent functional impairments and can thus lead to heart failure. In adult mammals, injured myocardial tissue forms a permanent, collagen-rich scar and damaged cardiomyocytes cannot generally be replaced. In contrast, some lower vertebrates, including salamanders and zebrafish, can efficiently regenerate heart injuries. In fact, unlike adult mammals, zebrafish adult CMs appear to be able to efficiently re-enter the cell cycle and to undergo cytokinesis and, thus, hyperplasia. While the cellular mechanisms of heart regeneration have begun to emerge, little is known about its molecular regulation and, in particular, the signals that regulate CM proliferation are still largely unknown. A better understanding of these mechanisms could be instrumental in efforts to improve heart repair in humans.

In our project, we plan to uncover the cellular and molecular function of the transcription factor Sox9a in zebrafish heart regeneration. A function of Sox9 in the development of the myocardium or in heart regeneration has not been described in any organism. Thus, we want to test the hypothesis that Sox9a is a key component of an injury-specific program regulating regenerative CM proliferation.

priv.

Fabian Bickel

Since the end of 2012, Fabian has been working at the Institute of Applied Biotechnology at Biberach University of Applied Sciences. He studied Biotechnology (BSc Esslingen University of Applied Sciences) and Pharmaceutical Biotechnology (MSc Biberach University of Applied Sciences and Ulm University). Given this background, he is well-equipped to solve both engineering and scientific problems.



Tamara Jacqueline Blätte

I was born in 1991 and moved to Ulm a couple of years ago to study Molecular Medicine. Having received my master's degree in May of this year, I am currently working on my PhD project in the Department of Internal Medicine III at Ulm University Hospital. In line with my previous studies, I am enrolled in the IGradU's program of Molecular Medicine.

Structure-activity relationship of protein stabilizing agents

On the one hand, protein aggregation is a well-known problem, especially in neurodegenerative diseases such as Alzheimer's disease. On the other hand, aggregation of monoclonal antibodies is a common issue in the biopharmaceutical industry. During the biopharmaceutical production process, there are certain stress conditions that can lead to protein aggregation, for example, stirring, temperature changes, certain ingredients, changes in pH, ionic strength, surface adsorption, shear forces, protein concentration, purity, morphism, pressure, freezing and drying.
The focus of our group (Prof. Kiefer) is the investigation of different aggregation model systems which mimic a certain process step. The focus of my work contributes to the salt-induced protein aggregation at low pH. This is an issue during protein A chromatography and virus inactivation. After a detailed characterization of the model system, the screening of protective additives was performed. Here, we used small molecules of the subgroups of polyols, amino acids and methylamines. With the generated dataset, a Quantitative-Structure-Activity Relationship (QSAR) should be performed. With this method, information about the protective properties of the molecules can be generated. As a final step, new compounds with more protective properties against protein aggregation can be designed

Genomic and transcriptomic landscape of acute myeloid leukemia

Acute Myeloid Leukemia (AML) is a heterogeneous disease characterized by the clonal expansion of myeloid progenitor cells. The World Health Organization (WHO) has defined multiple subgroups of the disease based on specific genomic aberrations present in the cancer cells. These subgroups are not only each associated with a certain prognosis but also with variable response to available treatment options. Thus, correct group allocation enables optimal patient care. However, even today, not all patients can be successfully cured. Therefore, it is necessary to further refine the classification system of AML and improve patient outcome.
This requires a thorough understanding of the genomic and transcriptomic landscape of the disease, a prerequisite to which my PhD studies aim to contribute. To that end, I will analyze different patient cohorts by DNA and RNA sequencing of matched diagnostic and remission samples. Initially, I will establish bioinformatics routines suitable for the analysis of such data. Then I will use these to analyze, across selected cohorts, the mutational profiles of patients and the changes thereof over time. This latter process, which is termed "genomic evolution of cancer," will be one of the main foci of my work. The integrative analysis of data from different sequencing technologies, namely, DNA and RNA sequencing as well as the available clinical data, will be another key aspect.

Johanna Blaha

Born in 1988. As part of the International Graduate School in Molecular Medicine Ulm, I am working on my PhD at the Institute of Transfusion Medicine (Director: Prof. Dr. med. H. Schrezenmeier) under the supervision of Dr. Klaus Schwarz.

priv.

Corinna Bliederhäuser

(née Wandhoff)

I was born in 1986. After studying Pharmaceutical Biotechnology at the Biberach University of Applied Sciences and at Ulm University, where I focused on basic research on hematopoietic stem cells as well as on acute myeloid leukemia for my bachelor's and master's theses, I joined the group of Junior Prof. Karin Danzer of the Department of Neurology, Ulm University, to pursue my PhD.

Analyzing a signaling defect in disturbed human NK-cell development

The examination of inborn errors of the immune system has contributed significantly to the understanding of the development of the human immune system and its function, including the elucidation of major signaling pathways. Very recently, the generation of human-induced pluripotent stem cells (hiPSCs) from primary dermal fibroblasts and the *in vitro* differentiation of hiPSCs into various cell compartments opened an avenue for disease-specific cellular models and analyses with otherwise sparse or unobtainable material.

Based on whole-exome and whole-genome sequencing data, candidate genes that may contribute to the unusual phenotype of an unexplored primary immune-deficient patient are being identified. With the help of CRISPR/Cas9 modified hiPSCs, we plan to explore the role and function of the previously identified candidate genes in the development of the immune system.

It is to be expected that the genetic analysis of unexplored primary human immunodeficiencies will elucidate signaling pathways involved in lymphocyte development and function. This knowledge will not only help to establish hiPSC-derived cell models but will also contribute to advances in hematology and oncology.

Characterization of monocyte subsets in PD patients and different mouse models for PD

Parkinson's disease (PD) is a multisystem neurodegenerative disorder. Emerging evidence points to a contribution of inflammatory processes to PD's pathogenesis, but implications of the peripheral immune system are still poorly understood. We therefore investigate the composition of monocyte sub-populations from PD patients and healthy controls via flow cytometry. Strikingly, we found a strong increase in the ratio of classical $CD14^+$ to non-classical $CD16^+$ monocytes in PD patients. Interestingly, similar results could be found in two different mouse models for PD. Human $CD14^+$ and $CD16^+$ monocytes correspond to $Ly6C^{hi}$ and $Ly6C^{lo}$ in mice. Notably, we found an increased ratio of $Ly6C^{hi}$ to $Ly6C^{lo}$ monocytes in $LRRK2^{(R1441G)}$ mice as well as in a Thy-1 αsyn-wt model, suggesting that different PD mouse models have a deregulation of monocyte subsets as a common feature.

We further investigated whether LRRK2 is differentially expressed in immune cells in PD patients. We found that LRRK2 is up-regulated in both monocyte subsets in PD patients, but no differences in LRRK2 expression was found for B cells, pointing to a specific role of LRRK2 in the monocytes of PD patients.

Christina Böck

Born in 1989, I am in the working group of Clinical and Biological Psychology at the Institute of Psychology and Education, and am part of the International PhD Programme in Molecular Medicine.

Characterization of cellular processes of aging following psychological stress in mothers with child maltreatment

The experience of child maltreatment, whether in the form of physical, emotional, or sexual abuse or in the form of physical or emotional neglect, can have detrimental effects on both the psychological and the biological development of a child, and is associated with long-lasting (mal)adaptations of diverse biological systems.
The aim of this PhD thesis is the characterization of psychoneuroimmunological alterations associated with the experience of child maltreatment in a study cohort of adult women, with a special focus on cellular processes of aging.
Due to the close interaction between the endocrine, the immune and the central nervous systems, which share the same bio-signaling molecules, the cells of the peripheral immune system are especially susceptible to the effects of (chronic) psychological stress. Child maltreatment is not only associated with an increased risk of psychological but also physical secondary disorders throughout life, including diabetes, allergies, cardiovascular diseases and even cancer. It is hypothesized that many of these co-morbidities, which are frequently observed in the setting of (chronic) psychological stress, have their roots in a disturbed function of the immune system. However, little is known so far about the underlying biological pathways and molecular mechanisms involved in the etiopathology of these biological consequences.

Elena Boldrin

Born in 1990 in Italy, she gained her bachelor's and master's degrees in Molecular Biology at the University of Padua, Italy. She is a PhD student in the Department of Pediatrics and Adolescent Medicine (group of PD Dr. Meyer), Ulm University Medical Center. She is part of the International PhD Programme in Molecular Medicine that is run in collaboration with the University of Padua which offers a doctoral course of studies in the Biosciences.

Impact of post-transcriptional regulation of gene expression in high-risk pediatric leukemia

The aims of this project are to investigate biological mechanisms of post-transcriptional and translational regulation of gene expression in B-cell precursor acute lymphoblastic leukemia (BCP-ALL). Patient-derived NOD/SCID/huALL xenograft samples, previously characterized for distinct engraftment phenotypes which are tightly connected to patient outcome, are analyzed by small RNA sequencing. RNAs, such as microRNAs and microRNA-offset RNAs, which are differentially expressed between the different biological subgroups are identified and related to patient outcome.
Small RNA expression data will then be integrated with gene expression profiles to investigate the effect of microRNAs in the regulation of genes affecting engraftment and outcome, which will then be confirmed by function in both *in vitro* and *in vivo* studies. Moreover, expression of long non-coding RNAs, including circular RNAs, will be studied to gain further insights into their role in post-transcriptional regulation of gene expression in ALL.
The overall aim of this study is to characterize regulatory networks in order to identify regulatory elements that might be new possible therapeutic targets.

Simon Breitenbach

I was born in 1981 and raised in Munich. I completed my bachelor's and master's degrees at WZW Weihenstephan, a part of TU Munich.
Currently, I work for Prof. Lehmann-Horn in the division of Neurophysiology. This is my third year at the Graduate School in Molecular Medicine here in Ulm.

Sarah Brockmann

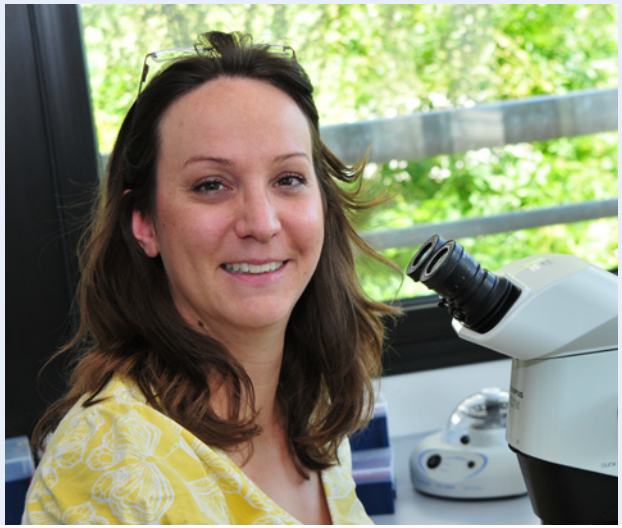
I was born in 1988 and studied Biochemistry at Ulm University. After completing my master's degree in 2014, I joined the working group of Prof. Dr. Jochen Weishaupt at the Department of Neurology. Recently, I was accepted on the Tissue Homeostasis Joint PhD Programme in cooperation with the University of Oulu (Finland), thus giving me the chance to receive a double degree.

Cause of membrane repolarization by steroids and hormones

Pseudohypertrophy, a swelling of the lower leg muscles especially and associated with a lack of muscle force, is a major symptom of Duchenne muscular dystrophy. Manifesting before the onset of the muscle's catastrophic transformation into fatty and connecting tissue, the underlying mechanism has remained inexplicable for two centuries. With a modern MRI protocol, we were able to demonstrate intracellular sodium retention of the muscle. This explained the depolarization of muscle fibers, reducing the ability to contract and also the swelling, due to the osmotic. We were able to remedy this with the potassium-sparing diuretic eplerenone. Its exact effect on the muscle is not described. In the diaphragm muscle fibers of *rattus norvegicus*, we were able to show a fast hyperpolarizing effect after administration of eplerenone. Furthermore, a chemically induced depolarization of the fibers was repolarized. The estrogen-derived eplerenone is a very specific blocker of the mineralocorticoid receptor. The MR, with its bound ligand aldosterone, is a functional transcription factor but also has fast, non-genotropic interactions. Aldosterone is described as an inhibitor of insulin signaling, thus an inhibitor of the IRS1/PI3K/Akt pathway and a regulator of SGK. This allows the MR to regulate the activity of an array of ion channels and transporters by localization and modification of phosphorylation. Besides the sodium-potassium-ATPase, sodium-chloride co-transporter, sodium-potassium-chloride co-transporter and sodium-proton exchanger are known targets of regulation by Akt.

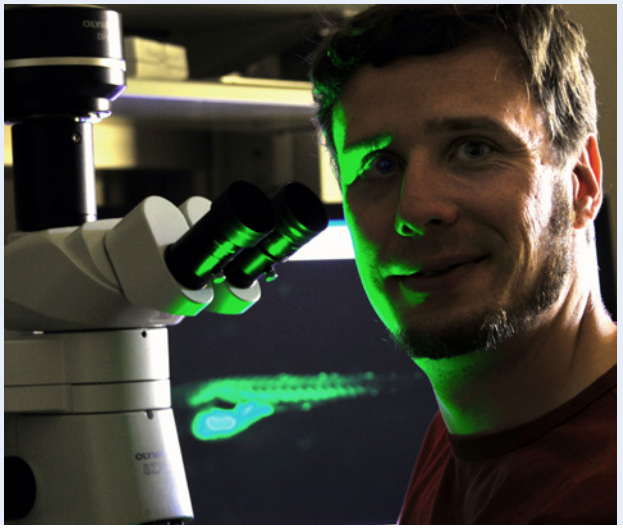
Functional screening for novel ALS candidate genes

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease affecting both upper and lower motor neurons. It is known for its rapidly spreading paralysis that finally leads to a patient's death from respiratory failure after an average of three to five years following diagnosis. So far, only about 50% of both familiar and sporadic gene mutations causing ALS are clarified. To improve this number, a large approach of exome sequencing of patient material retrieved from the Ulm ALS Biobank cohort was carried out. In this regard, we and others found a novel ALS disease gene called coiled-coil-helix-coiled-coil-helix domain containing 10 (CHCHD10). Up to date CHCHD10 is the first ALS gene directly associated with mitochondria. Apart from its mitochondrial location, very little is known about this protein.
The major aim of my PhD project is to characterize the molecular function of CHCHD10 in healthy persons as well as in ALS patients. Since we hypothesize that CHCHD10 might play a role in the regulation of the cellular respiratory chain, our intention is to analyze the mitochondrial function of the mutated protein and compare it to a wild-type control. That will lead to the question of the overall function of mitochondria in ALS. In a biochemical approach, we will use HEK293 cells, H4 (Human Neuronal Glioma cell line) and patient lymphoblasts as model systems to analyze interaction partners of CHCHD10. Moreover, zebrafish embryos will be used to study the function of CHCHD10 *in vivo*.



Anja Bühler

Born in 1986, I am a second year PhD student in the International PhD Programme in Molecular Medicine. I am working in the Department of Internal Medicine II (Molecular Cardiology). Our lab is mainly focusing on the genetic and molecular networks of heart development and function. The long-term goal of our research is the development of new therapies for heart/ muscle diseases.



John B. Bührdel

Born in 1982, I am a student in the International PhD Programme in Molecular Medicine and work in the Department of Internal Medicine II (Molecular Cardiology). Our lab is mainly focusing on the genetic and molecular networks of heart development and function. The long-term goal of our research is the development of new therapies for heart/ muscle diseases.

Targeting cardiomyocyte proliferation to enhance heart regeneration

Myocardial infarction in mammals leads to cardiomyocyte (CM) death, followed by the formation of an irreversible, noncontractile fibrotic scar and eventually heart failure. This inability to regenerate the damaged tissue is mainly due to the postmitotic state of mammalian CMs. In contrast, the zebrafish *Danio rerio* is able to resolve the scar and regenerate functional cardiac muscle tissue after injury. The impressive regenerative capacity of the zebrafish heart is due to the maintenance of a robust proliferative competence of resident cardiomyocytes in the adult fish. This involves cell cycle re-entry of spared cardiomyocytes, rather than the recruitment of cardiac stem cells. Only little is known about the molecular factors orchestrating heart restoration. To investigate the mechanisms controlling CM proliferation and regeneration, we characterized the zebrafish mutant, *baldrian (bal)*, which we isolated in an ENU mutagenesis screen. *Bal* mutants display a thin walled myocardium with less ventricular CMs. We identified a missense mutation in the Histone deacetylase 1 (HDAC1) gene. Histone deacetylases are epigenetic regulators, which remove acetyl groups from lysine residues on histone tails. HDAC1 plays an important role in mammalian embryonic development and cell cycle progression. The aim of this project is the characterization of the *bal* heart phenotype and the investigation of the detailed molecular mechanism by which HDAC1 regulates proliferation and cell cycle progression in embryonic zebrafish CMs.

Analysis of myofibrillar myopathy-related genes in zebrafish

Myofibrillar myopathies (MFMs) are a group of severe and progressive muscular diseases in humans. MFMs are caused by monogenic mutations in a variety of sarcomeric and extrasarcomeric proteins. Affected patients develop skeletal muscle myopathies, often severely affecting their life quality and expectancy. Today, the molecular mechanisms translating the genetic variation to the pathological phenotype are largely unknown. In order to test novel candidate genes and analyze the molecular mechanisms resulting in the MFM pathology, animal model systems are crucially important. To assess whether the zebrafish is a suitable model system, the known MFM-causing genes were inactivated utilizing antisense-mediated knockdown strategies. The resulting phenotypes were analyzed functionally and structurally. We consistently observed a myopathic phenotype with myofibrillar degeneration in the morphants. Similar to the situation in MFM patients, we found gene-specific pathologies, such as ultrastructural alterations of mitochondria and autophagic pathology. In addition, assessment of cardiac function revealed alterations specific to the targeted gene, including heart failure and arrhythmias. To further assess the zebrafish as a model system for MFM, we overexpressed wild-type and MFM-mutant human Filamin C in zebrafish, indicating the feasibility of this cross-species approach. In summary, our results indicate that the zebrafish is a suitable model organism to evaluate known and novel MFM disease genes.

Martina Sabine Burczyk

Born in 1988, Martina Burczyk is the first person in her family to attend university. After finishing her master's degree in Biochemistry at Ulm, she became a PhD student in the zebrafish lab of PD. Dr. Melanie Philipp at the Institute of Biochemistry and Molecular Biology. Martina joined the IGradU for the International PhD Programme in Molecular Medicine in 2013.

priv.

Andre Burkovski

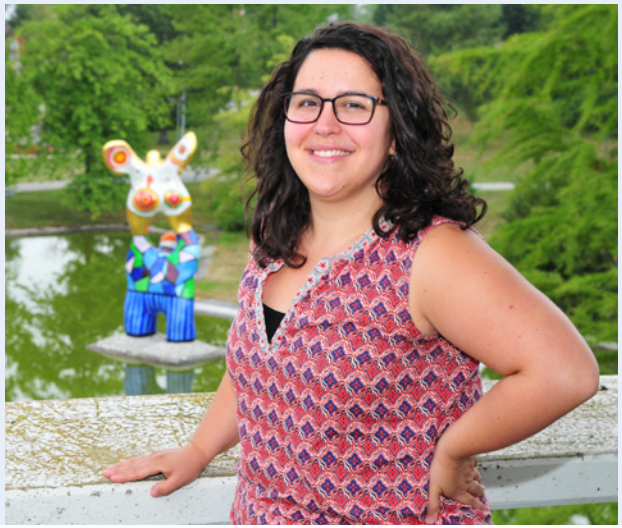
Born in 1982 in St. Petersburg, Russia. He studied Computer Science and Software Engineering at the University of Stuttgart with additional skills in Visualization and Machine Learning. Within the scope of his PhD project, he is now in the Kestler Lab at the Institute of Neural Information Processing to help uncover hidden patterns in biomedical data.

Human heart development explained using fish

Congenital heart defects are the most common developmental defects in newborns. They arise from exposure to environmental harms or through spontaneous or inherited variations in susceptibility genes. Heart defects can vary greatly in their morphology and, because of this, also in their severity. While less severe malformations heal by themselves, surgical attention may be required in more serious cases where the large vessels are connected unfaithfully or chambers are not septated. Unfortunately, the molecular causes of many heart defects have not yet been uncovered. In my PhD, I use small chemical compound screens to find key elements that drive proper cardiac differentiation and growth. In my studies, I use zebrafish embryos as a model that can be easily manipulated by immersion in water containing the chemicals of interest. Although the zebrafish heart is much simpler than a human heart, it nevertheless resembles closely the development and function of a human heart. Zebrafish have thus gained great acceptance in the field of molecular cardiology and have helped me to identify several exciting new key proteins that had not been associated with heart development so far.

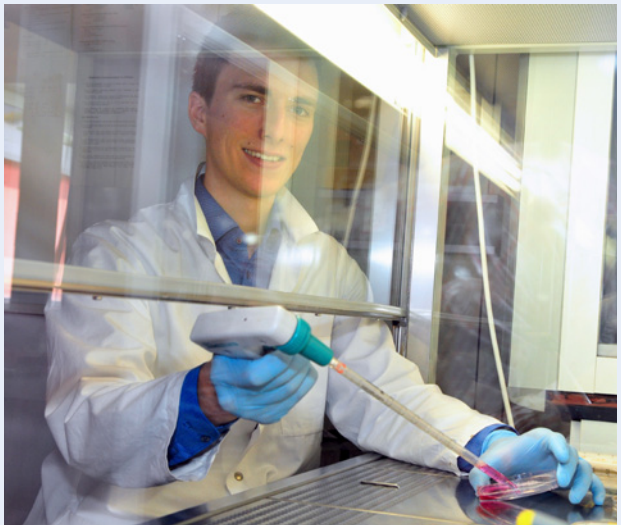
Classification and integration of high-throughput data

Many gene-expression studies include a large variety of model organisms and are meant to describe effects in different experimental conditions. Although single studies may show the desired effects, the integration of the individual study results can help to identify the common processes through data interaction. The main topic of my PhD thesis is the cross-platform and inter-species integration of gene expression data with the goal to uncover common processes and genes. Specifically, methods to combine ranked gene lists though rank aggregation procedures that produce a consensus ranking - a ranking with which all studies least disagree - are developed and their applicability is evaluated. Rank aggregation augments differentially expressed genes that are common across the individual studies and are shown to have high ranks in the resulting consensus ranking. The rank information in the resulting consensus ranking is further utilized in a novel gene set analysis. In such a way, it would be possible to identify common processes in gene expression data that are only discovered by the combination of different experiments. Additionally, rank aggregation methods can be used in order to improve the classification performance of prototype-based classification models.



Ilaria Cappadona

Born in1985. I first arrived in Ulm to complete my master's thesis (Erasmus Program) and then I stayed to pursue my PhD at the IGradU. I appreciated the way the IGradU supported our development not only in our specific field of research but in any branch of Molecular Medicine. This very well-structured program gave me all the tools to carry out a comprehensive PhD project.
Institute of Virology,
June 2011-August 2015



Stefan Carle

I was born in 1991 and am currently working at the Institute of Pharmacology and Toxicology in the research group of Prof. Dr. Holger Barth at Ulm University Medical Center. My work is funded by the International Graduate School in Molecular Medicine Ulm as part of a PhD program offered in cooperation with the University of Padua in the laboratory of Prof. Dr. Cesare Montecucco.

Regulation of human cytomegalovirus (HCMV) morphogenesis by the tegument protein complex pUL47/pUL48

Cytoplasmic stages of HCMV virion morphogenesis are completed at the vAC. The exact mechanisms of tegumentation and secondary envelopment at the vAC are unclear, but many results indicate an essential role for inner tegument proteins. pUL47 and pUL48 belong to the inner tegument and have been studied in alphaherpes viruses. Despite the great conservation among herpes viruses, the exact functions of pUL47 and pUL48 in betaherpes viruses and morphogenesis have not yet been elucidated.
The aim of my work was to reveal the role of pUL47 in HCMV morphogenesis and to clarify the functions of the complex pUL47/pUL48 in the late steps of HCMV assembly. The main goal was to generate a new model for HCMV assembly highlighting the central roles of the essential complex pUL47/pUL48. Our model is based on several observations from ultrastructural data, localization studies and the growth analysis of different mutant viruses: (i) unable to express pUL47; (ii) with mutations in the pUL47/pUL48 interaction domain; (iii) expressing Flag tag versions of pUL47; and (iv) with altered ability to associate with vAC membranes. In the long run, the main aim is to provide novel insights into the regulatory function that pUL47 and pUL48 exhibit in the late steps of HCMV maturation. The knowledge about the importance of this complex for the formation of infectious viral particles allows new possibilities regarding the development of new compounds targeting the essential steps of HCMV replication.

Toxin-mediated drug delivery across the Blood-Brain Barrier (BBB)

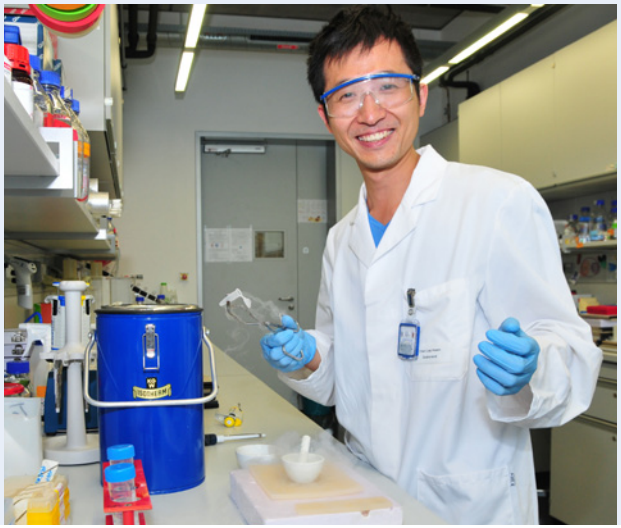
Neurodegenerative disorders, such as Alzheimer's disease, are a major issue in our aging society. Consequently, they are at the focus of modern drug development. However, the treatment of such diseases is limited by the strict barrier properties of the BBB that only allow the passive permeation of small, lipophilic molecules from the systemic circulation to the central nervous system and thereby prevent the effective delivery of most therapeutics. Different approaches for the non-invasive molecular circumvention of the BBB are currently in investigation.
Within this thesis, the transcytotic attributes of an enzymatically inactive diphtheria toxin mutant (CRM197), which has shown to penetrate the BBB, will be further explored. Additionally, optimization of the transport using certain pharmacological inhibitors (in collaboration with the University of Padua) will be analyzed. Therefore, *in vitro* transwell models using different cell lines will be established, mimicking, on the one hand, the endothelium of the BBB and, on the other hand, human nasal epithelium, concerning possible nose-to-brain delivery. After evaluation of the permeation across the transwell of the non-modified CRM197, a novel "molecular Trojan horse" based on the mutant will be developed using a streptavidin/biotin system to conjugate various cargo molecules to the protein. These conjugates will then be tested concerning possible transport within the transwell model, which could lead to a new tool for targeted drug delivery to the brain.

Teresa Casar Tena

Born in Madrid in 1987, she graduated in Biology from the University of Valencia and completed her master's in Molecular Approaches in Healthcare Science at the same university. After finishing her studies, she joined the International PhD programme in Molecular Medicine at Ulm University and started her PhD in the lab of PD. Dr. Melanie Philipp at the Institute of Biochemistry and Molecular Biology.

Novel key factors in symmetry breaking

The thesis focuses on how nuclear proteins regulate tubulin structures such as cilia and, with that, the establishment of left-right (LR) asymmetry. The events determining LR asymmetry are highly conserved among vertebrates and take place during early embryogenesis. Defects in the proper establishment of LR asymmetry are highly related to the development of Heterotaxy Syndrome, which is a condition that shows a random arrangement of the inner organs. In order to identify new factors guiding asymmetry development, a phosphorylation-sensitive mass spectrometry was applied to a zebrafish model of laterality defects. With this approach, several nuclear proteins were identified and are being investigated for their impact on cilia formation and function.



Lap Kwan Chan

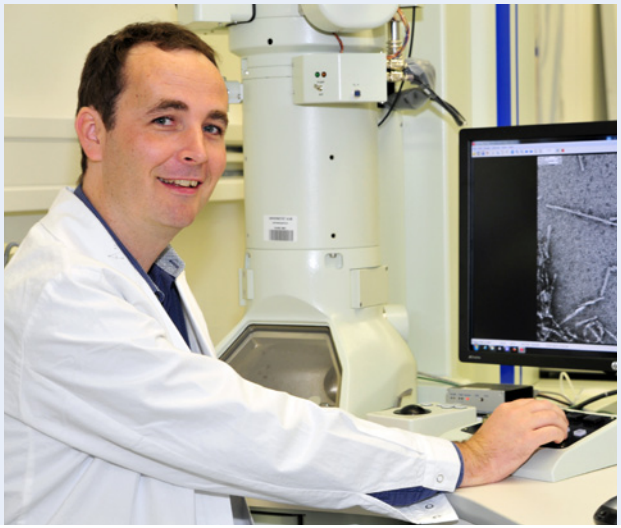
Born in 1983, I obtained a bachelor's degree in Biotechnology from the University of Hong Kong and a master's degree in Microbiology from the Chinese University of Hong Kong. In the spring of 2012, I joined the Institute of Physiological Chemistry as a PhD student and work closely with Prof. Dr. Thomas Wirth and Dr. Harald Maier. Currently, I am also part of the International PhD Programme in Molecular Medicine.

The role of NF-κB signaling in pancreatic diseases

My research interests are mainly concentrated on the exocrine pancreatic diseases, including pancreatitis and pancreatic cancer, by focusing on the contribution of the NF-κB signaling pathway. In my thesis, we combined a mouse model of pancreatitis and the different transgenic mouse lines lacking the specific components that are important for the activation of the NF-κB pathway (e.g. NEMO or IKK2). Interestingly, we found that the role of NEMO is context-dependent. During a recent study by our group showing that the absence of NEMO in the pancreas can reduce KRAS-driven tumorigenesis, as part of my thesis, we observed that its absence promotes the pathogenesis of pancreatitis. This means that NF-κB activation is, on the one hand, detrimental (pancreatic cancer) but, on the other hand, can also be beneficial (pancreatitis). Further understanding about the underlying mechanisms may help to reveal potential therapeutic approaches.

Dr. Resham Chhabra, PhD

Born in India in 1985, I undertook my PhD research project in the work group 'Molecular Analysis of Synaptopathies' in the Department of Neurology and graduated in November 2015. At present, I work as a postdoctoral research fellow in the laboratory of Dr. Philip C. Wong in the Division of Neuropathology at the John Hopkins University School of Medicine, USA.



William Close

Born in Australia, I grew up in Perth where I completed my undergraduate studies and then travelled to Germany where I am currently undertaking a research project at the Institute of Protein Biochemistry at Ulm University. The Molecular Medicine PhD program offered at the International Graduate School has provided me with a unique opportunity to pursue my scientific career.

Delivery of bioactive substances into the CNS using nanomedical approaches for the treatment of synaptopathies

During my PhD research, I investigated the use of polymeric nanoparticles (NPs) for the delivery of bioactive substances, such as proteins and zinc, into the CNS. The effective intracellular delivery of exogenous proteins is limited due to their instability and entrapment in the endo-lysosomal compartments of the cell. Thus, in order to design a novel system that could escape the endo-lysosomal compartments of the cell, we engineered novel hybrid NPs using the polymer, PLGA, conjugated with DOPE that is a lipid component known to disrupt lysosomes. We thoroughly characterized these novel hybrid systems and showed that these NPs could transiently disrupt lysosomes to release their cargo into the cytosol. Moreover, the approach does not appear to have cytotoxic effects. Furthermore, in the next part of the project, we investigated the use of NPs for the delivery of zinc into the central nervous system (CNS) across the blood-brain barrier (BBB). Zinc is now regarded as a potent therapeutic for various neurological disorders. However, the limited uptake of zinc into the brain, owing to the presence of the BBB, poses a serious challenge in selectively manipulating brain zinc levels, for example, by specific diets. Thus, in order to manipulate zinc levels within the CNS, we prepared zinc-loaded PLGA NPs conjugated with glycohexapeptide on their surface. This peptide was already shown to cross the BBB without any apparent damage. Using these NPs *in vivo*, we could show the targeted delivery of zinc into the CNS. In future, these novel established approaches will be used to deliver postsynaptic scaffold proteins and/or zinc into Alzheimer's disease models to investigate its therapeutic value in terms of the beneficial effect on synaptic pathology and/or behavior.

Revealing the three dimensional structure of amyloid fibrils via cryo-electron microscopy

Amyloidosis represents several diseases involving the accumulation of an abnormal protein, called amyloid. This misfolded protein forms amyloid fibrils which can be found in many organs, tissues and nerves resulting in organ dysfunction and ultimately death.
With the determination of the fibril structure we can gain many benefits such as improvements in the diagnosis and treatment of amyloidosis patients.
To achieve this, cryogenic electron microscopy is my method of choice to obtain high resolution micrographs of fibrils in their native form. These micrographs contain relevant information required for the reconstruction of amyloid fibril models at a near atomic resolution.
Computationally, these reconstructions require a large of amount of parallel processing power. Therefore, I am establishing computing facilities that are currently being optimised for the reconstruction of helical structures at our institute. With a close collaboration of the software developer of the Frealix reconstruction program at the Howard Hughes Medical Institute in the USA, I am confident to achieve a fibril model with an unprecedented resolution.
Bringing together laboratory sample preparation techniques, state of the art electron microscopy facilities and reconstruction methodologies, I am generating highly detailed fibril models with the intention to gain a better understanding of the molecular mechanisms that are involved, leading to the improvement of (early) diagnosis and treatment of this fatal disease.

Sibylle Cocciardi

Born in 1982, I completed my studies in Biology at Ulm University with the focus on Molecular Biology.
After my diploma degree, I worked for three years in Australia as a research assistant. In 2012, I joined the PhD Programme in Molecular Medicine to pursue my PhD in the Department of Internal Medicine III at Ulm University Hospital.

Barbara Commisso

I was born in 1988 and gained my master's degree in Molecular Biotechnology in Bologna, Italy. I joined the International Graduate School during the spring semester of 2015 and started working at the Department of Neurology under the supervision of Prof. Roselli. My PhD project focuses on the study of the contribution of astrocytes in ALS.

Clonal evolution and driver mutations in acute myeloid leukemia

In my PhD project, I use next-generation sequencing (NGS) to sequence the exomes of acute myeloid leukemia (AML) patients. AML is a genetically heterogeneous disease which is characterized by the accumulation of somatically acquired genetic alterations in hematopoietic stem/progenitor cells (HSPCs) that alter normal mechanisms of self-renewal, proliferation and differentiation. Several genetic markers have been identified to classify patients into prognostic groups which are used for treatment decisions. Nevertheless, many patients still have a poor prognosis and die from progressive disease after relapse. Recent efforts using NGS have identified additional mutations in genes, including *DNMT3A, IDH1, TET2* and *SF3B1*. However, most of the mutations found in AML genomes are actually random events that occurred in HSPCs before they acquired the initiating or founding mutation. To further elucidate clonal evolution in different AML subtypes, we are sequencing the exomes of AML patients at three time points: diagnosis; remission; and relapse. Following sequencing, we analyze the samples by using our in-house developed bioinformatics pipeline where the sequencing reads are aligned to a reference genome and the variants are called and annotated. The challenge is to identify mutations that cause the disease, contribute to disease progression and chemotherapy resistance, and/or cause the relapse, as opposed to mutations that are not relevant to the disease.

Neuronal components in ALS: networks in neurodegenerative diseases

Amyotrophic Lateral Sclerosis is characterized by degeneration of motor neurons initiating in mid-adult life. The ensuing progressive paralysis is typically fatal within four to five years and no treatment has been available so far. ALS is a non-cell autonomous disorder and a plethora of toxic mechanisms has been proposed to mediate pathogenesis. Astrocytes are major modulators of disease progression, but the precise contribution of glia to each stage of the disease is unclear since there are no tools to control glial cells *in vivo*. Astrocyte biology is controlled by calcium excitability and signaling cascades generated from membrane GPCR (G- protein coupled receptor). The activation of these receptors results in the activation of different pathways that regulate the communication between astrocytes and motor neurons. The idea is to manipulate astrocyte biology using a chemogenetic toolbox based on engineered GPCR. The result of this work may shed new light on glial contribution to neurodegeneration and provide an innovative tool to study glial physiology and pathophysiology *in vivo*.

Mohankrishna Dalvoy Vasudevarao

Born in 1983 in Bangalore, India, he studied Medicine at the Bangalore Medical College and Research Institute,India, and completed his master's degree in Biochemistry at the Jawaharlal Nehru Centre for Advanced Scientific Research, India.
Since 2012, he has been pursuing his PhD in the Weidinger lab at the Institute of Biochemistry and Molecular Biology, Ulm.

Elodie De Bruyckere

Born in 1989, she is doing her PhD under the direction of Prof. Stefan Britsch at the Institute of Molecular and Cellular Anatomy. She joined the IGradU in the spring of 2014.

Molecular mechanisms of zebrafish heart regeneration

Myocardial infarction is one of the leading causes of human morbidity and mortality. The typical response to infarction in mammals includes coagulation necrosis, inflammation and, finally, scarring with minimal replacement of the lost cardiomyocytes. However, certain species of amphibians and fish can effectively regenerate cardiac tissue upon various kinds of injuries. Significantly, the regenerative process includes replacement of lost tissue by cardiomyocyte proliferation. While efforts towards increasing cardiomyocyte proliferation in mammals post-infarction have not yielded definite molecular targets, it would be prudent to obtain clues from organisms that do naturally regenerate. For this purpose, we use zebrafish as a model system to identify factors that influence cardiomyocyte proliferation. The lab has generated data from high-throughput gene-expression assays which I employ to understand wound-healing and proliferation-based gene expression signatures. I characterize the temporal and spatial expression of a select number of genes that belong to a particular pathway by PCR and in situ hybridization-based analysis. I validate the function of gene/pathway in cardiomyocyte proliferation by the loss of function strategies, such as overexpression of dominant negative genes and small molecule inhibition. In this way, I hope to identify key molecular players that influence cardiomyocyte proliferation in zebrafish.

Bcl11b functions in the adult hippocampus

Bcl11b, a zinc-finger transcription factor, is expressed in several tissues of the mammalian body, including the brain. In the hippocampus, this expression is restricted to the postmitotic granule cells of the dentate gyrus and the pyramidal cells of the CA1 and CA2 regions. Previously, it had been demonstrated that Bcl11b plays an important role in hippocampal neurogenesis during postnatal development (Simon et al. 2012). The dentate gyrus is one of two regions of the brain where neurogenesis occurs throughout adulthood. Bcl11b is also expressed in adulthood, suggesting a role of Bcl11b in adult neurogenesis and/or the maintenance of adult hippocampal functions. The project of the thesis focuses on determining adult functions of Bcl11b in the hippocampus.

priv.

Juliane Charlotte de Vries

I was born in Düsseldorf, Germany, of a German mother and a Dutch father. My studies first took me to RWTH Aachen University where I received a diploma in Biology and, then, to Ulm to enroll in the International Graduate School in Molecular Medicine for my PhD. I am currently a PhD student in the Department of Dermatology and Allergic Diseases under the supervision of Professor Karin Scharffetter-Kochanek.

Jan Philipp Delling

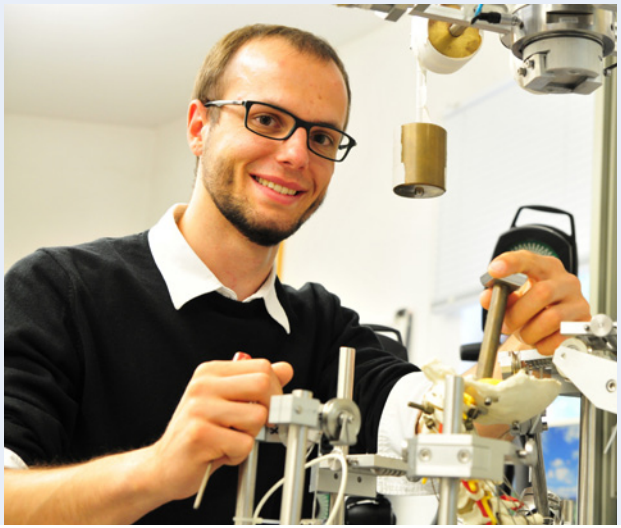
I was born in 1992. In July 2015, I began to work on my MD thesis at the Institute for Anatomy and Cell Biology under the supervision of Prof. Dr. T. Boeckers and Dr. Dr. M. Schmeisser. Since July 2015, I have been a participant in the study program in Experimental Medicine at the International Graduate School in Molecular Medicine Ulm.

Skin Aging and Adult Stem Cells

Adult stem cells are multipotent cells that self-renew within a specialized niche and differentiate exclusively into cell lineages of their tissue. They facilitate tissue homeostasis by replenishing dying cells and releasing various growth factors, thereby modulating the tissue microenvironment. Adult stem cells are defined *in vitro* by a marker panel in combination with plastic adherent growth and trilineage differentiation capacity. Therefore, investigation of their *in situ* behavior is severely hampered. I am working on a new population of adult dermal mesenchymal stem cells (MSCs) that are characterized by the exclusive expression of the p-glycoprotein ABCB5. Our group has previously reported a decrease in number and a change in niche preference of $ABCB5^+$ MSCs in the dermis of old individuals. I addressed changes in the niche itself and found an age-dependent decrease in the number of dermal perivascular cells expressing osteopontin, an extracellular matrix component, *in situ*. In culture, plastic adherent dermal cells sorted for the expression of ABCB5 robustly showed *in vitro* self-renewal capacity as assessed by colony formation and trilineage differentiation potential of single cell-derived cultures. Conversely, ABCB5-depleted dermal cell fractions did not even give rise to clonal cultures, thereby delineating the $ABCB5^+$ fraction as MSCs from $ABCB5^-$ human dermal fibroblasts (HDFs). In summary, the MSC marker, ABCB5, is a valuable tool for determining the mechanisms of stem cell aging *in situ* and *in vitro*, and to isolate MSCs easily and reliably.

The role of the Oxytocin-system in Shank-associated synaptopathies

My MD project focuses on characterizing the interplay between Shank molecules and neuropeptide systems, and, in particular, the Oxytocin (OT) system.
Shank proteins (*SHANK1-3*) are highly expressed in neurons and are considered to be crucial scaffolding proteins, especially at the postsynaptic density, but have also been found in other parts of the cell.
At our institute, we investigate the role of the *SHANK1-3* genes with respect to their association with Autism Spectrum Disorders (ASDs), a neuropsychiatric disorder with an early onset that is widely regarded as the result of synaptic dysfunction. Among the core symptoms of ASDs are restricted interests, stereotyped and repetitive behaviors, and deficits in social communication and social interaction. The neuropeptide OT has been identified as playing a major role in the mediation of social behavior, which suggests that treatment of a core symptom of ASDs might be possible through OT-related pathways. The OT system itself is also affected in some cases of ASDs.
Since Shank-associated mutations in rodents result in synaptic alterations, I characterize the effects of OT on synaptic parameters in rat cortical and hippocampal neurons. Furthermore, I will investigate a possible interplay between Shank proteins and the OT-receptor system on the protein and mRNA level. This will give a clue to the possible beneficial effects of OT in Shank-associated ASDs such as the Phelan-McDermid Syndrome (*SHANK3*-haploinsufficiency syndrome).



Robert Demmelmaier

Born in 1992, he is currently working at the Institute of Orthopedic Research and Biomechanics in the group of Prof. Dr. Hans-Joachim Wilke and is a member of the study program in Experimental Medicine. He initially started his study of Medicine at the Christian-Albrecht University of Kiel and is continuing his research at Ulm University.

Salih Demir

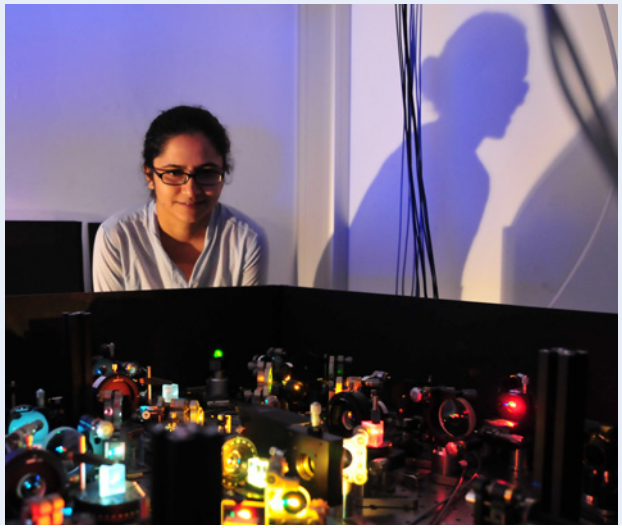
I was born in Turkey in 1988. I graduated from Gazi University and completed my master's at the Istanbul Technical University. I joined the International Graduate School in Molecular Medicine Ulm and entered its program in 2013. I am pursuing my doctoral studies at the Department of Pediatrics and Adolescent Medicine in the lab of PD Dr. L.H.Meyer.

In vitro examination to investigate the stabilizing effect of ligaments on ranges of motion at the cervical spine

The kinematics, as well as the anatomical and functional properties, of the cervical spine ligaments have not been completely illuminated. The assumption that the cervical spine behaves in movements directly comparable to the lumbar spine cannot be reenacted. The research at hand aims to define these properties and to provide the acquired data for the calibration process of a finite element model of the cervical spine which is currently in development at the Institute of Orthopedic Research and Biomechanics.
With the help of a spinal loading simulator, different functional spinal units will be examined. Through stepwise reduction of the components (i.e. the anterior longitudinal ligament, the facet joint capsule, and the flaval ligaments) and application of pure continuous moments in all planes, increasing ranges of motion will be measured. From comparison of ranges of motion after every step, each component's individual influence on cervical spine stability will be deduced and compared to all other component influences. The acquired data will help improve the understanding of the sharing of ligamentous stress in the cervical spine and will be compared to the behavior of the finite element model. This model will be useful for studying responses of the cervical spine to various loads and changes in kinematics due to treatments, such as artificial disc replacement, laminectomy, or fusion of functional spinal units, without the need for human specimens.

Targeting mutant p53 in pediatric acute lymphoblastic leukemia

Mutations of the *TP53* have been described as being associated with poor prognosis in different cancer types. *TP53* alterations are rarely present in acute lymphoblastic leukemia (ALL), but associations of mutated *TP53* with therapy resistance have been described. APR-246 (initially PRIMA-1^{MET}), a small molecule compound reported to restore *TP53* function, has shown activity in malignancies with mutated *TP53* (*TP53*mut). In ALL, mutant *TP53* has so far not been addressed as a therapeutic target.
In this study, we analyzed a cohort of 62 B-cell precursor (BCP) ALL primograft samples and identified four cases with *TP53*mut, at a frequency also reported in patient cohorts. In addition, two of six BCP-ALL cell lines analyzed were *TP53*mut. After this, we investigated the activity of APR-246 on *TP53*mut or wild type (wt) BCP-ALL cells lines and observed high sensitivity to APR-246 in *TP53*mut ALL with increased induction of apoptosis. Interestingly, upon APR-246 exposure, increased p53 phosphorylation and induction of the transcriptional targets NOXA and PUMA were detected in *TP53*mut but not *TP53*wt BCP-ALL cells.
In conclusion, *TP53*mut BCP-ALL can be targeted by APR-246 leading to p53 re-activation, NOXA and PUMA-mediated apoptosis and effective leukemia cell killing. Thus, targeting and re-activation of mutated p53 provides a promising novel therapeutic strategy in this high-risk subtype of BCP-ALL.



Dhruva KA Deshpande

Born in India, she came to Germany to study for a master's in Molecular Biotechnology at Bonn University and completed her thesis at the Forschungs–zentrum Jülich (Jülich Research Center). She remained in Germany to pursue her PhD in Molecular Medicine at the Institute of Biophysics, Ulm University. Her research interests lie in super-resolution fluorescence microscopy applied to biological systems. She can usually be found in her "dark dungeon" lab adjusting colorful lasers.

Elvira Dietrich

Born in 1992, I am a doctoral student in the study program in Experimental Medicine at Ulm University. Since August 2015, I have been doing my research at the Institute of Experimental Anesthesiology where I have been given the unique opportunity to participate in neurosurgery.

Implementing super-resolution microscopy techniques for protein localization studies

Super-resolution microscopy involves resolving structures smaller than the diffraction barrier and has revolutionized the field of fluorescence microscopy by enabling direct observation of biological processes, cellular architecture, and molecule interactions with high resolution. This thesis focuses on using the following three fluorescence microscopy techniques: direct STochastic Optical Resolution Microscopy (dSTORM); Photo-Activated Localization Microscopy (PALM); and STimulated Emission Depletion microscopy (STED).

The main project involves localizing synaptic proteins, such as FUS and TDP43, which are indicated in the pathogenesis of such neurodegenerative disorders as amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). As abnormal localization of synaptic proteins is shown to be important in disease progression, it is of interest to understand its distribution in normal synapses.

The role of natural CXCR4 ligands in Glioblastoma multiforme for infiltration by macrophages and sensibilisation of NK cells

Glioblastoma multiforme, a highly invasive and malignant primary brain tumor with poor survival rates, is the subject of my research. I investigate the role of the chemocine receptor, CXCR4, and its ligands in migration and growing of tumor cells. Dividing newly established cell lines into CXCR4 positive or negative lines by flow cytometry and immune histochemistry, I plan to cocultivate positive cell cultures with macrophages and NK cells with or without the presence of CXCR4 ligands, such as activating SDF-1‹ or a blocking albumine fragment called EPI-X4.

My aim is to show that CXCR4 stimulates proliferation and survival of glioblastoma muliforme, and that blocking this receptor could open a new way in treating this dangerous tumor.

Andrea Dietz

Born in 1991. During my studies in Technical Biology at the University of Stuttgart and my stay at the Georgia State University, I discovered my passion for working on human pathogen viruses. I am looking forward to being a part of the IGradU and the Institute of Virology.

Human cytomegalovirus morphogenesis as new antiviral target

The human cytomegalovirus (HCMV) is of prime importance as the most frequent viral cause of birth defects and severe diseases in immunocompromised hosts. Available antiviral drugs are limited to targeting the viral genome replication. Viral morphogenesis represents a good target for antiviral intervention because many of the processes involved in generating infectious virus particles are essential. However, this requires detailed knowledge of molecular mechanisms underlying the complex HCMV virion morphogenesis. We have recently identified viral proteins that regulate membrane envelopment of the cytoplasmic capsid: a crucial step in virion morphogenesis. The aim of the PhD project is to clarify the detailed mechanism of membrane envelopment during virion morphogenesis by a systematic analysis of selected viral proteins that are known to be involved in this process. This project is based on the hypothesis that these viral proteins form a complex, regulating membrane fusion and, thus, infectious viral particle formation. The analysis of the complex and the identification of relevant interactions between the complex partners, as well as the generation of mutant viruses and their characterization, will allow us to determine the relationship of the complex partners and the role of their interaction for virion envelopment and release. In addition, the determination of the interactome of these proteins will complete our molecular understanding of the membrane fusion process.

Johanna Duda

Born in 1986 in Groß-Strehlitz, Poland. As a member of the International PhD Programme in Molecular Medicine, I am currently in the last year of my PhD at the Institute of Applied Physiology (Prof. Birgit Liss). My research focuses on dopamine-releasing neurons and their role in health and diseases.

Converging roles of altered Ca^{2+} homeostasis, impaired DNA-integrity and mitochondrial dysfunction for selective neuronal vulnerability

Selective neuronal vulnerability is a key feature in CNS diseases. In my thesis, I analyze two proposed converging mechanisms for selective neuronal vulnerability in respective mouse models and human post mortem brains: imbalanced Ca^{2+} homeostasis and deficient DNA-integrity, which both lead to mitochondrial dysfunction and neuronal impairment. I focus on the differential vulnerability of dopaminergic (DA) neurons in Parkinson's disease (PD) and schizophrenia.
Using UV-laser microdissection and (RT)-qPCR, which enables mRNA/DNA quantification at the single cell level (Duda et al, in press), I detected reduced levels of distinct NMDA receptor subunits, specifically in VTA DA neurons in a schizophrenia mouse model (Krabbe, Duda et al, 2015).
Furthermore, I identified a transcriptional dysregulation of a signaling network of voltage gated Ca^{2+} channels, neuronal Ca^{2+} sensor, and D2-autoreceptor in SN DA neurons of distinct PD mouse models (Dragicevic et al, 2014; Poetschke et al, 2015).
By analyzing human post mortem brains, I identified specific genomic impairments in single SN DA neurons in PD patients compared to controls. My findings support the hypothesis of a self-accelerating vicious spiral of impaired Ca^{2+} homeostasis and DNA damage in highly vulnerable DA neurons in PD and schizophrenia, and/or leading to accelerating mitochondrial dysfunction, and triggering neuronal impairment and disease.

Konstantin Ehinger

Born in 1987, he works at the Institute of General Physiology. After obtaining his bachelor's and master's in Molecular Medicine at Ulm University, he continued his studies by entering the International PhD Programme in Molecular Medicine. In addition to his PhD work, he organizes a yearly scientific symposium for undergraduate students and is involved in Student Council affairs.

priv.

Verena Vanessa Emmerling

Born in Ulm in 1987, she studied Pharamceutical Biotechnology (BSc and MSc) at Biberach University of Applied Sciences and at Ulm University from 2006 to 2011. Since 2012, she has been part of the IGradU and is researching her PhD thesis at the Department of Gene Therapy, Ulm University, in cooperation with Rentschler Biotechnologie GmbH under the supervision of Prof. Stefan Kochanek.

Regulation of pulmonary surfactant secretion during the exocytic post-fusion phase

Regulated exocytosis of large secretory granules does not follow the classical steps of vesicle priming and fusion, fusion pore dilation, collapse into the plasma membrane, and passive release of vesicle contents. Increasing evidence suggests that for bulky, non-soluble vesicle contents, such as surfactant stored in lamellar bodies (LBs) of alveolar type II (ATII) cells, regulation of the post-fusion phase is critical for efficient secretion and, for this, active extrusion mechanisms are needed. The coating of fused vesicles with actin has been shown in a variety of cell types, including ATII cells, where post-fusion actin coating and subsequent vesicle compression have been shown to be essential for surfactant release. This process is dependent on the activation of Rho GTPases on the vesicle membrane after fusion. However, it is still unclear which members of the Rho family are involved and how vesicle fusion leads to GTPase activation. Regulators of Rho include guanine nucleotide exchange factors (GEFs), GTPase-activating proteins, and guaninenucleotide-dissociation inhibitors, which in turn are regulated by a variety of mechanisms, including membrane lipids and phosphorylation.

The aim of the project is the identification and characterization of upstream regulators of Rho GTPases during the LB fusion in ATII cells. We will analyze the role of various phosphoinositides, which are known upstream regulators of Rho. Furthermore, we will analyze and characterize GEF expression and involvement in the fusion process.

Recombinant Adeno-associated virus-based vectors for gene therapy: novel strategies towards improved manufacturing

Gene therapy has the potential to become a powerful clinical approach to address unmet medical needs in the future. Recombinant Adeno-associated virus (rAAV) represents one of the most promising viral vectors to be used in gene therapy-based treatment of monogenetic diseases. However, current strategies to produce rAAV vectors exhibit several bottlenecks that limit their applicability for efficient large-scale manufacturing. Within the scope of the thesis, approaches were developed and characterized to overcome the limitations of different rAAV production strategies. For this purpose, rational plasmid design was applied to enhance transient transfection-based production. In addition, the feasibility of a stable rAAV producer cell line was investigated by making use of RMCE and crucial mechanisms involved in vector production from stable cell lines were identified. Furthermore, cultivation temperature was optimized and temperature-induced cellular changes were examined to explain the pro-productive effect. Finally, profiling of miRNAs overexpressed during conditions favoring rAAV production identified a miRNA which was shown to enhance rAAV productivity. Comprehensive characterization revealed this miRNA to be highly suitable for cell line engineering.

Deborah Katharina Erhart

Born in Friedberg (Bavaria) in 1991, I have been studying Medicine at Ulm University since 2011. For my dissertation, I became a member of the Molecular Biology Research Laboratory and focus on Oncology under the direction of Dr. Claudia Friesen at the Institute of Forensic Medicine. In 2015, I entered the doctoral study program in Experimental Medicine (Promotionsprogramm Experimentelle Medizin) at the IGradU.

Katharina Ernst

I was born in 1986 in Warburg. After completing my studies in Biology in 2011 at Ulm University, I continued my research work in the lab of Prof. Holger Barth at the Institute of Pharmacology and Toxicology as a PhD student. I joined the International PhD Programme in Molecular Medicine of the IGradU and graduated in August 2015.
My project was funded by the DFG (Grant BA 2087/2-2 to H.B.).

The development of new therapy strategies for gastric cancer by using opioids and, especially, D,L- Methadone

Gastric cancer is counted as being among the ten most frequent tumor localizations in Germany. The peak of incidence lies between the fifth and sixth decade of life.
The five-year survival rate depends on the stage it is at and lies between 70 and nearly 0-5%.
For chemotherapeutic treatment, cisplatin, 5- fluoruracil, capecitabine and irinotecan are often used. If the palliative prognosis is fatal, it will be necessary to discover alternative new therapeutic strategies to increase the response to therapy and to aid recovery.
The aim of this dissertation thesis is to research whether the opioid, D, L- Methadone, is able to intensify the sensitivity of gastric cancer to chemotherapeutic substances (cisplatin) as A.G. Friesen has already shown in some further experiments with glioblastoma and leukemia. Activation of μ-opioid receptors by the receptor agonist, methadone, enhances the effect of the substances and overcomes already existing resistances. This project is focused on the molecular mechanisms of apoptosis. The mitochondrial (intrinsic) and ligand- receptor (extrinsic) signal transduction pathway needs to be examined. Therefore, a commonly used method is, inter alia, western blot analysis with antibodies against the main actors of apoptosis, e.g. Bcl-2 and Bcl-x_L for extrinsic pathway, and initiator caspases 8 and 9 and executioner caspase 3 for the final common path. For quantification of the apoptosis rate, I intend to use flow cytometry as described by Nicoletti.

The requirement of host cell chaperones and peptidyl-prolyl *cis/trans* isomerases for membrane translocation of bacterial ADP-ribosylating toxins in mammalian cells

Bacterial ADP-ribosylating toxins belong to the group of AB-type toxins that consist of a B-domain which facilitates binding and translocation of the enzymatically active A-domain. After entering the target cell via receptor-mediated endocytosis, the B-domain forms a pore in the membrane of acidified endosomes and the A-domain is partially unfolded to translocate across the membrane into the host cell cytosol. In the cytosol, the A-domain covalently transfers an ADP-ribose moiety onto a specific substrate, which leads to cellular reactions and severe clinical symptoms of, for example, diphtheria, cholera or whooping cough. It is worth noting that these symptoms can be prevented if the membrane translocation can be inhibited. The aim of my thesis was to characterize the membrane translocation of ADP-ribosylating toxins concerning the requirement of host cell chaperones and peptidyl-prolyl *cis/trans* isomerases (PPIases), which are important protein folding helper enzymes of the cell. During my thesis, I identified the PPIases FK506 binding protein 51 and Cyclophilin 40 as well as the heat shock protein Hsp70 as novel interaction partners of ADP-ribosylating toxins during their membrane translocation. It is important that the identification of required host cell factors serves as a starting point for the development of novel therapeutic strategies aimed at inhibiting toxin translocation and, therefore, preventing clinical symptoms.

Vida Farsam

I was born in December 1984 and started my PhD studies under the supervision of Prof. Karin Scharffetter-Kochanek in April 2012 in the Department of Dermatology and Allergic Diseases.

Kristin Anja Feder

Born in 1990, I grew up in a village near Heilbronn and moved to Ulm in 2009 to study Biochemistry at Ulm University. I completed my master's thesis on the role of the Thioredoxin-interacting protein in human AML at the Institute of Experimental Cancer Research and was accepted as a PhD student in January 2015. In April 2015, I started the Graduate School's program.

Role of senescent fibroblast secretome on the progression of cutaneous squamous cell carcinoma

Cutaneous squamous cell carcinoma (cSCC) represents the second most common type of skin cancer worldwide with an increased propensity for local recurrence and metastasis. The incidence of cSCC dramatically increases with age due to accumulation of mutations in stem/progenitor cells and, as recently proposed, due to senescence-associated pro-oncogenic changes in dermal stroma. Our group has previously reported that the number of p16INK4a positive senescent human dermal fibroblasts (HDFs) probably reveals a senescence-associated secretory phenotype (SASP) that increases in human skin during aging. I am addressing the question whether and how the SASP of HDFs affects the major hallmarks of cSCC progression such as enhanced cell motility and invasion. The SASP of HDFs was systematically analyzed using RNA profiling and ELISA. Higher concentrations of chemerin, a chemotactic factor, were detected in senescent compared to young fibroblasts *in vitro*, and were confirmed in situ by using skin samples derived from old compared to young human individuals. Chemerin enhanced the migration of cSCC cell lines *in vitro* through activation of the MAPK signaling pathway. These results will be further explored *in vivo* in the context of cSCC progression. Our studies will contribute to the understanding of the effect of factors secreted from senescent fibroblasts on cSCC cell migration and progression, and may allow us the perspective to develop strategies to counteract the tumor-promoting properties of senescent fibroblasts.

Dissecting the role of Lymphoid Enhancer Factor 1 in hematopoiesis and acute myeloid leukemia

For my PhD thesis, I investigate the role of Lef1/LEF1 in hematopoiesis and AML. Lef1 is a 54kDa protein of the Lef/Tcf family of transcription factors and is, for example, involved in Wnt signaling. It is already known that Lef1 is relevant for murine HSC and progenitor function. Retroviral constructs, which overexpress the Lef1 protein lacking the DNA-binding domain or lacking the β-catenin-binding domain (Lef1Δ56), were designed and it was found that DNA binding of Lef1 is important at the level of short and long-term repopulating stem cells. The β-catenin-binding ability only plays a role in the case of short-term repopulating stem cells. To examine if Lef1 and Lef1Δ56 act on different pathways, ChIP-Seq was performed and a very interesting candidate emerged: Wnt5a, which is involved in non-canonical Wnt signaling. LEF-1 lacking the β-catenin-binding domain is known to be highly expressed in most immature human HSCs and suppresses canonical Wnt signaling (Nature 2013, Anjos-Afonso et al.) and that this isoform is highly expressed in aged LT-HSC in parallel to high Wnt5a expression (Nature 2013, Florian et al.). My task in this project is to investigate whether the overexpression of Lef1Δ56 suppresses gene expression of the canonical Wnt pathway and increases the expression of non-canonical Wnt genes. I will also examine whether Lef1Δ56 overexpression changes the localization of β-catenin and Wnt5a. Finally, I will examine the role of LEF1Δ56 in human AML.

Marisa Feiler

Born in 1987, I completed my bachelor's degree in Pharmaceutical Biotechnology at the Biberach University of Applied Sciences in 2010. Subsequently, I entered the master's program in Pharmaceutical Biotechnology at Ulm University and, during this time, I also spent ten months completing my master's thesis in Boston. Currently, I am doing my PhD in the Department of Experimental Neurology in the lab of Prof. Weishaupt.

priv.

Eva-Maria Feldmann

Born 20 July 1979, she works at the Department of Otorhinolaryngology (Head and Neck Surgery) at Ulm University Medical Center. She is also taking part in the International PhD Programme in Molecular Medicine.

Development and characterization of a TDP-43 aggregation assay to study the transmission of TDP-43

TDP-43 is an aggregation-prone prion-like domain-containing protein and component of pathological intracellular aggregates found in most ALS patients. TDP-43 oligomers have been postulated as releasing and subsequently nucleating TDP-43 oligomerization in recipient cells, which might be the molecular correlate of the systematic symptom-spreading observed during ALS progression.
The first aim of my PhD project was the development and characterization of a novel protein complementation assay to allow quantification of TDP-43 oligomers in living cells. After the successful set up of the assay, we further used the assay to demonstrate the presence of TDP-43 oligomers in microvesicles/exosomes and showed that microvesicular TDP-43 is preferentially taken up by recipient cells where it exerts higher toxicity than free TDP-43. Moreover, we established microfluidic neuronal chambers in our lab, which allows us to study TDP-43 axonal transmission. Our findings suggest both anterograde and retrograde trans-synaptic spreading of TDP-43. Furthermore, we wanted to study whether TDP-43 can seed further TDP-43 oligomerization/aggregation using our assay. We were able to demonstrate TDP-43 oligomer seeding by TDP-43 derived from both cultured cells and ALS patient CNS tissue extracts.

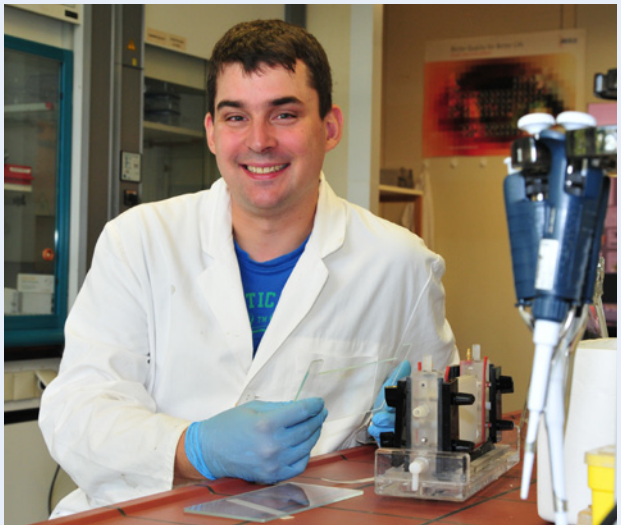
Ear tissue regeneration using human cells and bacterial nano-cellulose

We investigated bacterial nano-cellulose (BNC) as a novel biomaterial for its aptitude as implant material for ear cartilage tissue engineering. BNC is produced by *Gluconacetobacter xylinus*. To evaluate the influence of the scaffold, which differs in production process and composition with alginate, several prototypes have been tested. Human primary chondrocytes obtained by routine reconstructive septorhinoplasties were used for 3D longterm culture. Cell adhesion, distribution and proliferation were analyzed. Cartilage neo-synthesis was evaluated on the protein and gene expression level.
Some prototypes proved to be more suitable for application in auricular cartilage tissue engineering. Therefore, detailed focus was set on BNC 1st, BNC 5th and BNC 7th. BNC 1st was successfully tested as a vascular graft substitute but provided insufficient shape stability for auricular reconstruction. BNC 5th combined the benefits of BNC and alginate. It showed good shape stability and cell infiltration abilities. BNC 7th, a bilayered scaffold, combined biochemical and biomechanical characteristics necessary for successful auricular cartilage regeneration.
Computer-aided design techniques were applied to facilitate the production of custom-made, patient-individual implants. Therefore, MRI was used for the discrimination of cartilage, adipose and skin tissue in the auricle. Subsequently, a 3D structure was designed for producing a negative ear mold. The scaffold (BNC 7th) was then produced by using this mold to form the individual shape.
Acknowledgment: ERA-NET/EuroNanoMed.

priv.

Simon Fischer

I was born in Tettnang, Germany, in 1985. I studied Pharmaceutical Biotechnology (BSc) and Biomedical Engineering (MSc) at the Biberach University of Applied Sciences and the Albstadt-Sigmaringen University of Applied Sciences, respectively. During the last three years (2012-2015), I prepared my PhD thesis at the Institute of Applied Biotechnology (IAB), Biberach.



Stephan Fischer

I was born in 1984 in Laupheim. After school, I spent four years in the German Armed Forces before studying Bio- and Process Engineering at Furtwangen University and Biochemistry at Ulm University. After finishing my master's thesis in the group of Prof. Holger Barth, I remained there as a PhD student. In April 2015, I joined the International PhD Programme in Molecular Medicine.

Next-generation cell engineering of biopharmaceutical production cells using microRNAs

Biopharmaceuticals are complex biological drugs which must be produced by living systems. Chinese hamster ovary (CHO) cells represent the predominantly employed host cells for the production of biotherapeutics. However, CHO cells exhibit bottlenecks regarding cell growth, stress resistance or productivity, and are thus steadily improved by genetic engineering. The aim of my dissertation was to precisely elucidate the role of a novel class of small non-coding RNAs, so-called microRNAs (miRNAs), in CHO production cells in order to find novel opportunities to enhance cell performance in biopharmaceutical production processes. Therefore, I screened >1100 different miRNAs for their ability to improve culture performance. Strikingly, we could identify hundreds of novel miRNAs which were demonstrated to enhance protein production, cell growth or resistance to cell death. Even more interestingly, we showed for the first time that a large number of miRNAs actually controls several completely different cell functions concomitantly, which underscored the important role of these tiny RNAs in mammalian cells. In addition, we were able to partly elucidate target genes and pathways of some of these impactful miRNAs in CHO cells, which enabled us to unravel the biological processes leading to the observed superiority. In conclusion, our findings greatly helped to improve the fundamental understanding of miRNA-mediated gene regulation in CHO cells.

Characterization of the uptake mechanism of bacterial protein-toxins and their inhibition by human peptides

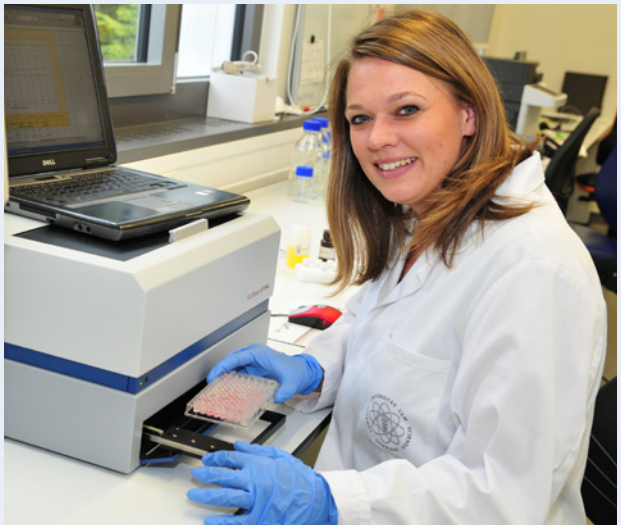
Bacterial AB-type toxins are secreted by living bacteria and act independently from the producing bacteria. They belong to the group of exotoxins and enter surrounding tissue via a very efficient uptake mechanism, including receptor-mediated endocytosis. In the cytosol of the target cells, they act as enzymes and cause cell damage, which results in typical symptoms of several severe diseases such as diphtheria, botulism or whooping cough. Given the lack of agents effective against antibiotic-resistant bacterial strains and bacterial exotoxins, the development of novel pharmacological strategies is needed. In recent years, it was shown that human antimicrobial peptides, as part of the immune system, play a crucial role not only in inactivation of bacteria but also in inhibition of bacterial toxins. Furthermore, the screening of human peptide libraries revealed unexpected and unknown activities of peptides against bacterial pathogens.
Prompted by these results, the aim of my PhD thesis is the identification and the characterization of novel human peptide-based inhibitors against bacterial toxins in close collaboration with U-PEP and the Institute of Organic Chemistry III. To address this objective, the screening of a human hemofiltrate-derived peptide library providing a huge diversity of biologically active peptides, as well as the anti-toxin activity of human defensins as important effectors of our innate immune system against various bacterial exotoxins, will be investigated.

Philip Förstner

I was born in 1989 and studied Biology from 2009 until 2015 at Ulm University. My bachelor's and master's studies were both mainly focused on Molecular Biology. Recently, I have started the research for my doctoral thesis at the Institute of Physiological Chemistry in the working group of Prof. Dr. Knöll and have joined the PhD program of the Graduate School.

The impact of traumatic brain injury on neuronal integrity and nerve regeneration: gene expression, mechanisms and neuroprotective strategies

A traumatic brain injury (TBI) caused by an external impact can lead to transient or persisting cognitive and physical impairments, and even to death. The research of my PhD project focuses on the consequences of TBI on neuronal functions and especially on the role of the neuroprotective transcription factors, SRF and ATF3, in recovery after several TBI time points. Therefore, I perform gene-expression analysis and investigate the motor- and neuro-behavioral recovery of mutant and wild-type mice after TBI. I also use histological techniques to analyze the effects of TBI on neurocellular processes, such as neuronal survival, axonal degeneration, axonal transport and growth, as well as dendrite complexity. In addition, I am interested in other TBI-affected processes, including myelination, blood brain barrier leakage, edema and hemorrhage formation, and brain immune responses.



Sandra Förtsch

Born in 1988 in Bamberg. I obtained my bachelor's and master's degrees in Biology at the University of Regensburg. In 2014, I started my PhD project in the Laboratory for Molecular Psychosomatics at the Clinic of Psychosomatic Medicine and Psychotherapy, Ulm University Hospital, under the supervision of Prof. Dr. Stefan Reber. In 2015, I joined the IGradU.

Effects of chronic psychosocial stress on the sympathetic nervous and the cardiovascular system

Chronic, in particular, chronic psychosocial stress is known to be a risk factor for numerous somatic and affective disorders. However, in both humans and rodents the development of either affective or somatic, especially cardiovascular, disorders varies highly between individuals. Due to the lack of appropriate animal models, the underlying mechanisms are far from understood and, thus, the possibility to clinically benefit from these observations is currently still limited.
Furthermore, continuous visual (sensory) contact to the stressor might be responsible for whether established chronic stress-induced somatic and/or affective pathologies ameliorate, persist or even aggravate over time.
In my study, I use the chronic subordinate colony housing (CSC) paradigm, a preclinically validated model for chronic psychosocial stress in male mice. Detailed behavioral analysis revealed individual differences among CSC mice and that while some mice show more active stress-coping behavior, others show more passive ones. One aim of my study is to investigate whether there are chronic stress-induced changes in the cardiovascular and the sympathetic nervous system and if these changes are influenced by individual coping strategies. Another part of my thesis deals with the possible chronification of the CSC-induced changes at the level of the cardiovascular and sympathetic nervous system and if this further depends on the visual and/or olfactory/auditory contact to the stressor.

Ann-Kathrin Fuchs

Born in 1987, she is doing her PhD at the Institute of Pharmacology of Natural Products and Clinical Pharmacology. Before coming to Ulm University, she completed her bachelor's and master's theses in Biological Sciences at the University of Constance and studied abroad for one year at the University of Toronto. Her main areas of interest are cancer and immunological research.

Jan-Bernd Funcke

Born in 1988, he studied Molecular Medicine at Ulm University from 2008 to 2013 and joined the International Graduate School in Molecular Medicine Ulm in 2014. At the Division of Pediatric Endocrinology and Diabetes, his research focuses on age-associated changes in adipose tissue function, especially functional alterations in the adipose stem and progenitor cell compartment.

Exploration of amino-functionalized gold nanoparticles for therapeutic applications in acute myeloid leukemia

Acute myeloid leukemia (AML) is a malignancy of the myeloid lineage of the hematopoietic system. Even though it only accounts for 2% of all cancer cases, it still contributes highly to the number of cancer-related deaths. To date, the gold standard treatment consists of cytarabine and daunorubicine as a combination chemotherapy, which was already established in 1973. In particular, older patients often cannot tolerate the strong chemotherapy, which results in a very low five year survival rate in patients over 65 years of age.

During the last couple of years, nanomaterials evolved as a versatile tool in nanomedicine. So far, their main applications lie in diagnostics although more and more studies are investigating their use as therapeutic agents.

The aim of my PhD project is to investigate the potential of amino-functionalized gold nanoparticles ($AuNH_2$) in the treatment of AML. These particles seem to selectively target leukemia cells and induce cell death. Previous data suggest that healthy cells of hematopoietic progeny are resistant to $AuNH_2$. We would like to proof-differential sensitivity of transformed and healthy cells towards amino-functionalized gold nanoparticles, *in vitro* and *in vivo*. Furthermore, we want to understand the mechanism of cell death and the molecular basis for selective sensitivity towards $AuNH_2$. With this, we hope to contribute to the development of new therapies for AMLthat are more selective towards tumor cells.

Influence of age on adipose tissue plasticity

Adipose tissue is a highly active endocrine organ and central regulator of systemic health. With age and with obesity, alterations in the function and distribution of adipose tissue occur and have been associated with the development of conditions such as insulin resistance, diabetes mellitus type 2, and cardiovascular disease.

Adipose tissue plasticity is tightly linked to the functionality of local stem and progenitor cells. A loss of functionality of these cells, especially those in the subcutaneous depots, has been hypothesized to underlie the alterations in function and distribution observed with aging and obesity.

Not much is known about the mechanisms maintaining the functionality of the stem and progenitor cells found in adipose tissue, especially not about the influence of adipose tissue secretion products, which are collectively referred to as adipokines, on these cells.

This project aims at identifying adipokines relevant to the long-term maintenance of adipose tissue stem and progenitor cell function, characterizing the patterns of their secretion and investigating the mechanisms of their actions.

Niklas Christopher Gäbler

Born in 1992, he is a medical student at Ulm University. In February 2015, he started his MD in the Division of Pediatric Endocrinology and Diabetes in the Department of Pediatrics and Adolescent Medicine. For his work, Niklas is in the study program in Experimental Medicine.

Angiogenesis in the development of adipose tissue in children

Throughout life, the increase and decline of adipose tissue are accompanied by the growth and maturation of blood vessels that provide oxygen and nutrients to the tissue. To ensure adequate vascularization, adipocytes and their progenitors, the preadipocytes, are capable of secreting proangiogenic factors which promote vessel growth. Interestingly, Tang et al. (2008) have shown that the preadipocytes themselves rest in the perivascular region. This indicates that adipogenesis (differentiation of preadipocytes to adipocytes) and angiogenesis (formation of new blood vessels) occur at the same location simultaneously. This interdependence of adipogenesis and angiogenesis in adipose tissue is supported by findings made in 1983 by Poissonet et al. that have shown that, during fetal development, the sprouting of a capillary is the first step in the formation of fat lobuli. Throughout childhood, the growth and functionality of the adipose tissue change multiple times, which suggests intense regulation.

The aim of this project is to identify differences in the angiogenesis in adipose tissue of children and their correlation with age and weight. To address this question, adipose tissue samples are obtained in collaboration with the Division of Pediatric Surgery of the Department of General and Visceral Surgery from children undergoing surgery, and the RNA expression of angiogenic factors in the tissue is measured. Furthermore, the proliferative and differentiation capacity of the tissue cells is examined. The results are then analyzed together with the anthropometric data of the patients.

Simeon Gaessler

Born in 1990, he has been studying Medicine at Ulm University since 2011 and is a member of the scholarship study program in Experimental Medicine at the International Graduate School in Ulm. Currently, he is doing his medical doctoral thesis at the Institute of Molecular and Cellular Anatomy at Ulm University.

The role of Bcl11a/Ctip1 and Bcl11b/Ctip2 in neocortical development

It has been shown that both zinc-finger transcription factors, Bcl11a and Bcl11b, play important roles in the development of the neocortex. Bcl11a is necessary for migration and survival of upper-layer cortical projection neurons, whereas Bcl11b is critical for correct differentiation of subsets of deep-layer neurons. Bcl11a is expressed by many projection neurons throughout the neocortex, while Bcl11b is restricted to deep-layer projection neurons. Both genes are coexpressed to a large extent in deep cortical layers. It is not known whether Bcl11a and Bcl11b have redundant functions and can compensate for each other.

In my project, I investigate forebrain-specific conditional Bcl11a//b compound mutant mice. The phenotype analysis demonstrates a major shrinkage in cortical thickness, aberrant development of deep-layer neurons, and indicates compensatory functions of Bcl11a and Bcl11b.

Felix Gassert

Born 1992 in Weinheim, he has been studying Medicine at Ulm since 2011 and has worked on his PhD thesis since March 2015 in the Orthopedics Clinic in the Section of Biochemistry for Joint and Connective Tissue Diseases. He is also in the study program in Experimental Medicine.

Franziska Gehringer

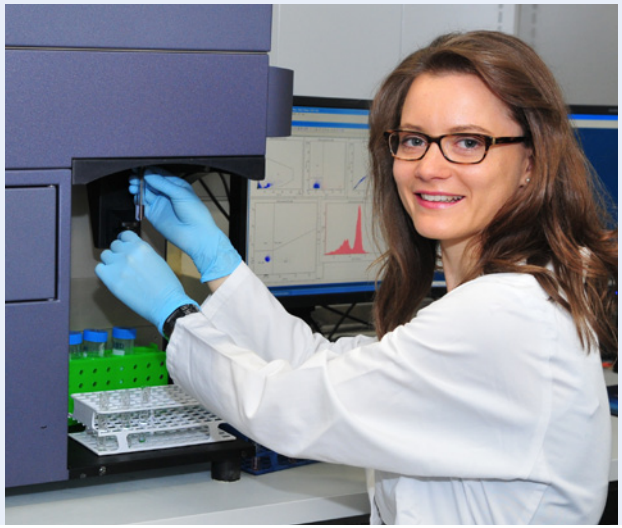
I was born in 1989 and grew up in Weinstadt, east of Stuttgart. I received both my BSc and MSc in Molecular Medicine from Ulm University and these laid the foundation for entering the IGradU in April 2015. Currently, I am pursuing my PhD studies at the Institute of Physiological Chemistry under the supervision of Prof. Dr. Thomas Wirth and Dr. Alexey Ushmorov, and am focusing on B cell lymphoma and leukemia.

Tissue regeneration in a bovine *in vitro* cartilage trauma model: analysis of therapeutic effects

Joint injuries, including cartilage trauma, are some of the main risk factors for developing posttraumatic osteoarthritis. An early pharmacologic treatment could possibly reduce initial articular damage and promote regenerative processes. Former studies have shown that the antioxidant agent N-Acetylysteine might have positive effects on cell viability and that the growth factor IGF-1 might support regenerative processes.
The effects of N-Acetylcysteine and IGF-1 on traumatized cartilage will be examined using a bovine *in vitro* model. A drop-tower model is used for traumatization. Analyses include histological stainings, immunohistochemistry, gene-expression analysis, live/dead staining, DMMB assay and the Boyden chamber assay.

Targeting FOXO1 for treatment of B cell precursor acute lymphoblastic leukemia (BCP-ALL)

FOXO1 plays an important role in B cell differentiation, particularly in early B cell development. Whereas FOXO1 was shown to be downregulated and to function as a tumor suppressor in classical Hodgkin lymphoma and mediastinal B cell lymphoma, it is highly expressed in BCP-ALL cells. Recently, our group found that both FOXO1 knockdown by shRNA and treatment with the low molecular weight FOXO1 inhibitor AS1842856 induced apoptosis in BCP-ALL cells, indicating an oncogenic role of FOXO1 in BCP-ALL. The goal of my project is to investigate the contribution of FOXO1 to the oncogenic program of BCP-ALL and to explore the mechanism of the selective anticancer activity of AS1842856 in BCP-ALL.
It has been hypothesized that AS1842856 binds to the FOXO1 transactivation domain, potentially leading to disruption of the interaction with co-activator proteins.
By conducting SILAC (stable isotope labeling by amino acids in cell culture), we aim to identify the influence of AS1842856 on the FOXO1 protein interactome in BCP-ALL cells. Moreover, we are planning on identifying AS1842856-interacting proteins.
This study will help to understand the oncogenic role of FOXO1 in BCP-ALL. Identification of FOXO1-interacting proteins may facilitate the development of new therapeutic agents by specifically targeting pro-survival FOXO1 interactions.



Eva Gentner

Born in Germany in1988. After receiving the General Higher Education entrance qualification, I decided to study for both a bachelor's and master's in Biology at Ulm University. I then entered the International Graduate School in Molecular Medicine to perform the experiments for my PhD thesis that I am conducting at the Institute of Experimental Cancer Research under the supervision of Prof. Dr. Christian Buske.

Manuel Gey

Born in 1982 in Langenau, Germany. After finishing my diploma in Biology at the University of Hohenheim, I started my PhD studies at Ulm University. Currently, I am in the fourth year of my PhD studies in Molecular Medicine at the Institute of Physiological Chemistry under the supervision of Prof. Bernd Knöll.

Dissecting the role of the homeobox gene VENTX in normal and malignant hematopoiesis

Homeobox (Hox) genes are key factors in the development of acute leukemias. However, little is known about the role of non-clustered Hox genes such as VENTX. VENTX is a member of the Vent gene family in mammals. It is known that VENTX overexpression in $CD34^+$ human stem cells promotes myeloid differentiation and it shows an aberrant expression in human acute myeloid leukemia (AML) characterized by the AML1-ETO (AE) fusion. To prove the functional role of aberrant VENTX expression in this AML genotype, we mimic high expression of VENTX in murine bone marrow (BM) progenitor cells. In contrast to AE, coexpression of AE+VENTX induces an AML after a median latency of 11.3 months which is retransplantable. Massive infiltration of erythroblasts in the spleen is documented. Blasts in BM express CD19, partly in combination with Sca1 and Gr1, and point to an aberrant expression of this antigen in the AE/VENTX leukemias. *Ex vivo*, leukemic cells grew permanently by generating AE/VENTX positive cell lines. RNA-Seq analyses from $CD34^+$ cord blood transduced with VENTX documented 279 differentially expressed genes compared to GFP control, hitting seven pathways in the KEGG-Analysis and showed a downregulation of genes necessary for terminal erythroid differentiation (e.g. EPO-R and GATA1). These data characterize VENTX as an important contributing factor to AE positive leukemias and allowed the generation of a murine AE model. Ongoing analyses are trying to elucidate the regulatory network of VENTX and its seven pseudogenes.

The role of the transcription factor ATF3 in axon regeneration after facial nerve injury in the mouse

Upon neuronal injury, the expression of many genes is induced. A subset of these genes is called regeneration-associated genes (RAGs) which represent an injury-induced network of genes. The induction of the RAGs is lower in the central nervous system than in the peripheral nervous system. The peripheral nervous system has higher regenerative abilities and the induction of the RAGs may correlate with regeneration, although the influence of a single RAG on regeneration could be rather low. RAGs are a heterogeneous group of genes with different functions which also include transcription factors. One of the transcription factors belonging to the RAGs is the activating transcription factor 3 (ATF3). Transcription factors are of high interest because they potentially orchestrate the RAG response and can control the expression of many RAGs at once. To further investigate the role of ATF3 in peripheral nerve regeneration, I employ the facial nerve lesion model to compare the regeneration of the facial nerve in *Atf3* knockout mice and wild-type mice.

Alina Glebova

Born in 1993 in Riga, Latvia, I am pursuing my medical doctorate at the Institute of Applied Physiology under the supervision of Prof. Birgit Liss. I am a participant in the study program in Experimental Medicine and in the "Neuro-Track" program. I have always been fascinated by the (dys-)function of the nervous system and have thus chosen to work in a research group that focuses on the dopamine midbrain system.

Oliver Vinzenz Glomb

I was born in 1989 and graduated in Biochemistry at Ulm where I completed my master's thesis at the Institute of Molecular Genetics and Cell Biology. I remained at the institute to begin my PhD thesis in September 2015.

Stereological quantification of numbers of dopaminergic neurons during aging in distinct mouse models with deficient calcium signaling

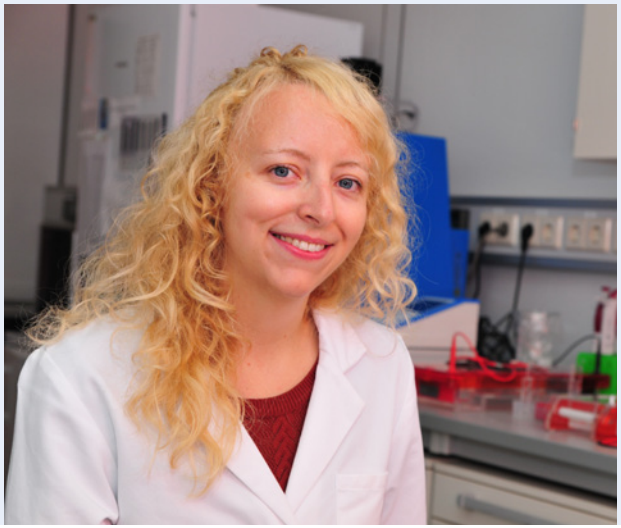
Aging is a major trigger factor for Parkinson's disease (PD). The neuropathological hallmark of PD is the selective, progressive loss of dopaminergic neurons in the substantia nigra (SN DA), while those of the neighboring ventral tegmental areal (VTA) remain largely unaffected by the disease. Although the cause of this differential vulnerability of DA neurons is still unclear, altered calcium signaling seems to play a crucial role. It is especially the activity of voltage-gated L-type Ca^{2+} channels (LTCCs) selectively in SN DA neurons that seems to render them more vulnerable to degeneration, and pharmacological LTCC blockers are already in clinical trials as novel PD-therapy. Our own group has recently identified that a subtype of LTCCs called $Ca_v1.3$ can, in a complex interplay with other voltage-gated calcium channels (VGCCs), sensitize D2-autoreceptor responses in SN DA neurons in an age-dependent manner via the neuronal calcium sensor NCS-1. Therefore, in my thesis I will quantify the numbers of SN DA and VTA DA neurons at different ages (young, adult and aged -PN13, PN90 and > PN370) in WT mice and in KO mice, where this signaling pathway is affected: NCS-1 KO, $Ca_v1.3$ KO, as well as other VGCC KO mice.
After sectioning and immunohistochemistry for tyrosine hydroxylase, I use the stereology for unbiased cell number quantification, and *ImageJ* for quantification of SN DA and VTA DA axonal fibers within the striatum which is their projection area.

The yeast polarisome as a nucleus for organizing the cytosol at the cell tip

Asymmetric growth is a fundamental aspect of cellular life. We aim to understand the protein interaction networks which are involved in asymmetric cell growth and division by using the baker's yeast *Saccharomyces cerevisiae* as a model organism. Genome-wide interaction screens uncovered plenty of protein-protein interactions, but their biological interpretation is not straightforward. *S.cerevisiae* divides by asymmetric cell division in a process termed budding. In late G1 phase, the growth of the mother cell is hereby directed towards the tip site, resulting in the formation of a bud. The bud expands and finally separates, leading to the generation of a smaller daughter cell. A protein interaction network named the polarisome plays an important role in this process. Throughout the directed growth, the polarisome stays sharply concentrated at the bud tip, disassembles upon isotropic growth and reassembles at the bud neck at the onset of cytokinesis. The deletion of any of its core components results in the same rounded cell phenotype. Furthermore, the core proteins have been shown to interact with proteins involved in cell polarization, cytoskeletal organization, organelle inheritance and further mechanisms. I want to decipher how the polarisome is coordinated and, in turn, how it coordinates all these mechanisms involved in asymmetric cell division.

Annika Verena Goß

I was born in 1988 in Goslar, Germany. I studied Biology (BSc) in Marburg and subsequently Biomedicine (MSc) in Hannover until 2013. Afterwards, I applied for a PhD position in the laboratory of Prof. Dr. C. Beltinger at the Clinic of Pediatrics and Adolescent Medicine. I have been a student of the International PhD Programme in Molecular Medicine at Ulm since April 2014.



Stefanie Grabrucker

Born in 1982, Stefanie is a PhD student at the Institute for Anatomy and Cell Biology, and a member of the International Graduate School in Molecular Medicine at Ulm University. Her research focuses on molecular and behavioral characterization of autism mouse models.

Attenuated oncolytic measles virus against acute lymphoblastic leukemia of childhood: preclinical proof-of-principle and molecular mechanisms

Leukemia is the most frequent pediatric cancer and acute lymphoblastic leukemia (ALL) is the most common subtype. Although the five-year event-free survival rate for children with ALL is more than 80%, diseased adults and the majority of relapsed children still have a poor prognosis. Oncolytic viruses selectively replicate in and kill cancer cells. Preclinical data published by Prof. Dr. Christian Beltinger show that attenuated measles virus (MV) efficiently replicates in and kills human T- and B-precursor ALL cell lines *in vitro*, as well as pediatric primary and xenograft B-lineage ALL cells *ex vivo*. In contrast, only limited sensitivity of peripheral blood mononuclear cells towards attenuated MV, with no effect on hematopoietic stem cells, was detected. The different sensitivity is neither due to differential expression of the common MV cell entry receptors nor differences in the transcriptional MV-induced antiviral interferon response. The aim of my PhD thesis is therefore to find key molecules and pathways by a genome-wide screening in human B-precursor ALL cell lines using the novel CRISPR/Cas9 technology and deep sequencing. *In vitro* studies of selected candidates in these cell lines will provide evidence for their impact on attenuated MV infection, replication and cell kill. Novel insights into the molecular mechanisms of the differential sensitivity will support future clinical translation of attenuated MV against leukemia.

Molecular and behavioral characterization of autism mouse models

My research focuses on the characterization of novel mouse models for autism spectrum disorders (ASD). ASD comprises neurodevelopmental disorders characterized by their core symptoms: delayed acquisition of speech; deficits in social interactions; and stereotypic behaviors. Multiple molecular genetic studies in the past have provided evidence that the pathogenesis of ASD has a strong genetic component. However, although genetic factors might be largely responsible for the occurrence of ASD, they cannot fully account for all cases. It is likely that in addition to a combination of ASD-related genes, specific non-genetic factors act as risk factors triggering the development of ASD. Thus, in my work, I investigate whether altered SHANK signaling (by genetic ablation, reduction due to knockout of RICH2, a SHANK interactor, or environmentally induced) leads to specific behavioral phenotypes associated with ASD. Mutations/deletions of SHANK genes have already been identified as genetic risk factors for ASD in patients. A non-genetic factor, especially prenatal zinc deficiency, is included in the focus of my research given that Shank proteins are highly zinc dependent.

Sarah Grasedieck

I was born in 1986 and have lived in Saxony-Anhalt, Brandenburg and Bavaria. I have studied in Berlin, NRW, Baden-Württemberg and California. I started my PhD in 2012 in the group of Dr. Florian Kuchenbauer (Department of Internal Medicine III) and have acted as a student representative for the IGradU since 2013.

Non-coding RNAs as biomarkers for CNS diseases

The aim of my PhD project is to create an atlas for miRNAs and long non-coding RNAs in human cerebrospinal fluid (CSF) based on a variety of central nervous system (CNS) diseases. In addition, we explore the potential of both non-coding RNA species to serve as biomarkers for diseases such as Alzheimer's disease or multiple sclerosis. Using a combination of highly sensitive quantitative real time PCR and high-throughput RNA sequencing, we screened miRNAs in 92 patient samples (discovery set) that cover the major CNS-related disease classes (autoimmune, neurodegenerative, inflammatory, and malignant). Next, we will validate the obtained miRNA data in independent patient cohorts to identify sensitive and disease-specific miRNA signatures. The long-term goal of this project is to create customized diagnostic qRT-PCR arrays which are: (i) suitable for a large spectrum of neurological diseases; (ii) easily integrated into clinical routine; and (iii) require only a small amount of patient material (CSF or serum).

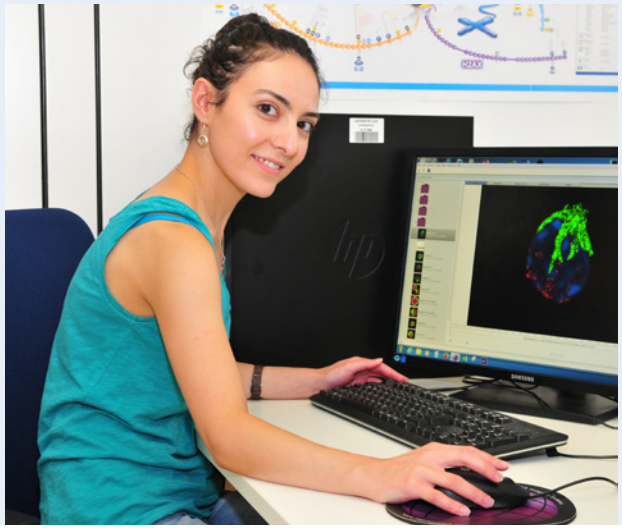
priv.

Melanie Grieb

Born in 1980, I am working in the Core Group of Medical Systems Biology headed by Professor Kestler.
I am currently finishing my PhD at the International Graduate School in Molecular Medicine Ulm.
I majored in Computer Science, with a minor in Biology, and worked for many years as a software developer before starting my PhD here in Ulm.

Gene regulatory networks with a Boolean network extension incorporating uncertainty

A Boolean network (BN) is a model of a gene regulatory network. In a BN, a gene is modeled as either activated (1) or deactivated (0). To model uncertainty in a BN, a Boolean Network Extension (BNE) was created which allows continuous values in the interval I = [0, 1]. As the transition functions of a BN can only be applied to Boolean values, the Boolean logic was converted to product-sum fuzzy logic. The resulting model is characterized by discrete time and continuous variable values. Fixed points of the BNE can be used to predict biological phenotypes by mapping the continuous fixed point of the BNE to the Boolean fixed point with the closest distance by using nearest neighbor matching. The BNE model was applied to the BN model of cardiac development, which models the differentiation of cardiac progenitor cells in the mesoderm during gastrulation into two different lineages called first heart field and second heart field. The simulation of the BN model with the BNE revealed additional phenotypes which could be confirmed by experiments in Xenopus.



Ani Grigoryan

I was born in 1988 in Armenia. I am a PhD student of the International Graduate School in Molecular Medicine at the Institute of Molecular Medicine.

Nuclear organization in HSC aging

The project is focused on investigating changes in the nuclear architecture of hematopoietic stem cells upon aging as it is this that might undergo spatial reorganization and contribute to aging and aging-associated diseases.

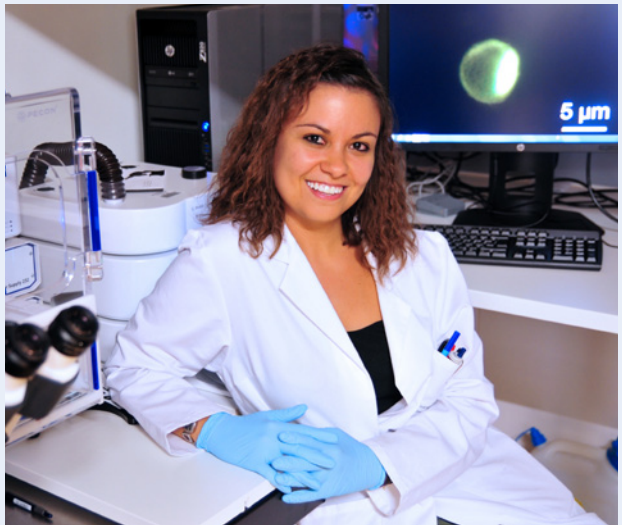
priv.

Veselin Grozdanov

I was born 1987. After pursuing a BSc degree in Molecular Medicine, I graduated with a MSc in Biochemistry at Ulm. My interest in the fields of Neurology and Immunology, as well as the possibility of combining basic research with clinical science, brought me to the lab of Junior Prof. Dr. Karin Danzer at the Institute of Experimental Neurology where I am studying Parkinson's disease as the focus of my PhD thesis.

Peripheral innate immunity in Parkinson's disease

In my PhD thesis, I am studying the peripheral innate immunity in Parkinson's disease and during healthy aging. Parkinson's disease, which is the second most common neurodegenerative disease, leads to severe motor disability as well as autonomous dysfunction. Increasing evidence points towards pathological processes in the peripheral immune system of Parkinson's disease patients in parallel to pathology in the central nervous system. We are focusing on peripheral blood monocytes, the effector cells of the peripheral innate immunity. Monocytes from Parkinson's disease patients display a pathological phenotype, characterized by altered gene expression, abnormal cytokine expression, and decreased phagocytic capacity. We are also studying the effect of alpha-synuclein, a protein which is directly involved in the pathogenesis of Parkinson's disease, on blood monocytes. In my thesis, I utilize a broad range of methods for studies of cellular function, immune response and gene expression to address the question of how the peripheral innate immunity is connected to the disease pathology of Parkinson's disease.



Novella Guidi

Born in 1985 in Milan, Italy, Novella has been carrying out her PhD project at the Institute of Molecular Medicine and Stem Cell Aging of Ulm University since February 2012.

Melanie Haffner-Luntzer

Born in 1987, she is a junior researcher at the Institute of Orthopedic Research and Biomechanics at Ulm University. She received her bachelor's and master's degrees in the field of Molecular Medicine from Ulm University in 2009 and 2011, respectively. In March 2015, she finished her PhD thesis at the International Graduate School in Molecular Medicine.

A role for stroma-derived osteopontin in hematopoietic stem cell aging

Upon aging, HSCs undergo changes in function and structure, including skewing to myeloid lineages, lower reconstitution potential and loss of protein polarity. While stem cell intrinsic mechanisms are known to contribute to HSC aging, little is known on how aged-related changes in the BM niche regulate HSC aging. We thus hypothesized that HSC niches age and that these aging-associated changes impair HSC function. Interestingly, we revealed that, upon aging, stroma cells present with a reduced amount of osteopontin (OPN), a secreted glycoprotein expressed by osteoblasts located close to the endosteum. Functionally, exposure of young HSCs to an OPN knockout stroma *in vivo* resulted in a decrease in stem cell engraftment, an increase in LT-HSC frequency and a loss of stem cell polarity. Moreover, a brief *ex vivo* exposure to OPN fragments functionally rejuvenates old HSCs, resulting in increased engraftment, decreased HSC frequency with increased polarity and restored balance of lymphoid and myeloid cells in peripheral blood. Our data therefore suggest a critical role for reduced stroma-derived OPN in promoting aging-related phenotypes on HSCs.

Role of midkine during fracture healing

Although the treatment of long-bone fractures was clearly improved over the last decades, the rate of delayed bone healing or even non-union formation is still up to 10%. The exact knowledge of the complex process of bone healing and the factors involved is a prerequisite for the development of new therapeutic strategies to prevent delayed healing. Melanie's PhD thesis investigated the role of the growth and differentiation factor, midkine (Mdk), during fracture healing. Furthermore, the question of the direct effects of Mdk on the fracture-healing-related cell types of chondrocytes and osteoblasts was addressed *in vitro*. The results of the present study demonstrated an important and complex role of Mdk during fracture healing and diverse mechanisms of action depending on the cellular location and the addressed cell types. The study indicates that application of the Mdk-Ab during fracture healing carries high therapeutic potential to enhance regeneration in patients with orthopedic complications such as non-union formation or delayed bone healing.

Yvonne Hägele

Born in 1991, she did her bachelor's studies in Molecular Medicine at Ulm University. For her master's studies in Molecular Medicine, she went to Uppsala University in Sweden where she graduated in 2015. Since October 2015, she has been enrolled in the International PhD Programme in Molecular Medicine of the IGradU. She is currently working at the Institute of Orthopedic Research and Biomechanics.

Benedikt Haggenmüller

Born in 1992, he is a medical student at Ulm University. After his first state examination, he became interested in Endocrinology and therefore started his doctorate in the Division of Pediatric Endocrinology and Diabetes in the Department of Pediatrics and Adolescent Medicine. Currently, Benedikt is a member of the study program in Experimental Medicine.

The role of the complement system in bone homeostasis and under inflammatory conditions

The complement system is an evolutionary ancient system, which is part of the innate immunity, and is crucial for host defence by bridging the innate and adaptive immune systems. The complement system supports, among others, the phagocytosis of pathogens and the production of inflammatory cytokines. However, an over-activation of complement can be detrimental, leading to prolonged inflammation and subsequent tissue destruction. In recent years, clinical evidence has accumulated and indicates that the complement system is involved in several acute and chronic inflammatory disorders.

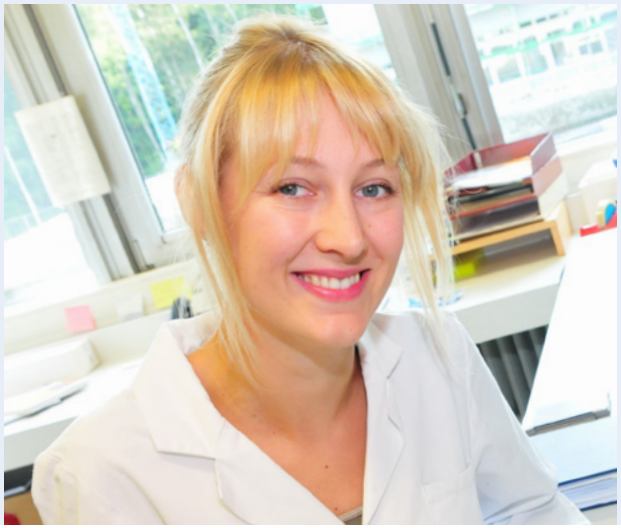
Complement is also anticipated to be crucially involved in bone remodeling, a process determined by a dynamic balance of bone formation and bone resorption. As a consequence, the anaphylatoxins, the main inflammatory effector molecules of the complement system, seem to be of great importance. In support of this theory, the receptors of the anaphylatoxins have recently been found to be expressed in bone cells. However, little is known about the molecular mechanisms and transduction pathways in bone cells that are induced by complement and its activation products. Therefore, this project aims to examine the effects of complement on bone formation during bone cell differentiation and maturation, both under physiological and inflammatory conditions.

Influence of immune cells on browning of white adipose tissue of children

The existence of functionally relevant brown adipose tissue (BAT) in human adults has been accepted in the scientific community since 2009. In contrast to the energy-storing white adipose tissue (WAT), BAT utilizes energy to generate heat. Recent data demonstrated that BAT activity is reduced in obese patients. Therefore, it has become an attractive pharmacological target for the treatment of obesity and overweight patients. Besides white and brown adipocytes, a third adipocyte type has recently been described, namely, the beige adipocyte. In mice, this cell type emerges under certain circumstances within the WAT depot and is called "browning," The cellular and molecular basis for the recruitment of beige adipocytes in humans is only poorly understood. However, both brown and beige adipocytes are thermogenic and can contribute to an increase in energy expenditure. Recent studies performed in mice demonstrated that browning of WAT depends on the presence of eosinophils and alternatively activated macrophages (Nguyen et al., Nature 2011; Qiu et al., Cell 2014). The aim of my project is to elucidate a possible relationship between these immune cells and the formation of beige adipocytes in WAT in both children and adults.

Simone Hagmeyer

Born in 1989. I am currently engaged in the working group of Molecular Analysis of Synaptopathies at the Neurocenter of Ulm University under the supervision of Jun. Prof. Dr. Andreas Grabrucker. I joined the International Graduate School in Molecular Medicine in April 2015.



Sonja Halbedl

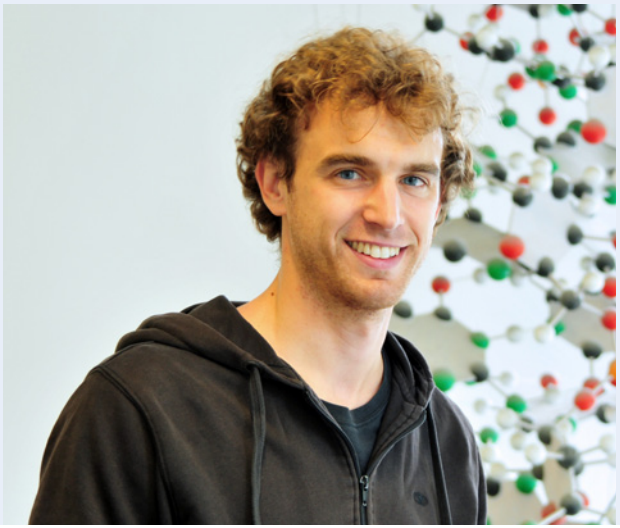
I was born in September 1983 and joined the Graduate School in Molecular Medicine Ulm in October 2012 after finishing my diploma thesis in Developmental Biology. Currently, I am in my last year as a PhD student at the Institute for Anatomy and Cell Biology under the supervision of Prof. T. Boeckers and Dr. Dr. M. Schmeisser.

Investigation of neurochemical and biological modulators of zinc signaling and protein accumulation at excitatory synapses of the central nervous system

Reduced brain function and restricted neurophysiology are hallmarks of age-dependent dementia. Protein aggregates that are deposited, either within or outside of neurons during aging processes, lead to neurological dysfunctions. In particular, the accumulation of extracellular aggregates disturbs synaptic activity. However, the formation of protein aggregates in the brain extends over a long period of time. The occurrence of these proteotoxic damages in the healthy brain must therefore evoke gradual changes in the neuronal protein network. On the other hand, protein aggregates can also occur during brain development and, in this instance, protein aggregates may trigger neuropsychiatric disorders rather than a neurodegenerative disease.
In this project, we focus on the influence of protein aggregates, especially S100B proteins, on synaptic proteins. We want to analyze by which mechanisms proteins accumulate in the brain and how this process influences synaptic function and, especially, how an altered zinc homeostasis and its induction of synaptic protein network alterations are crucial for the development of neuronal dysfunction. Furthermore, we will investigate how the age of onset influences the outcome of alterations on a synaptic level. In particular, we want to analyze changes in the synaptic environment and variation on synaptic proteome due to S100B protein-mediated proteotoxic insults.

Characterization of Shank2 function in development and disease

All three Shank family members (Shank1, Shank2 and Shank3) are essential scaffold proteins of the postsynaptic density (PSD) of excitatory glutamatergic synapses. In the PSDs, Shank proteins multimerize and build large molecular platforms, thus providing multiple protein-protein-interaction sites. These platforms link postsynaptic receptors with their downstream signaling proteins and the actin cytoskeleton of dendritic spines. So far, each of the Shank genes has been associated with Autism Spectrum Disorders (ASD).
My PhD project focuses on the characterization of several novel Shank2 brain region-specific knockout (KO) mouse lines which are all based on the targeted mutation in the full germline Shank2 KO mouse that was published in 2012. It has been shown that germline Shank2 KO mice display increased locomotor activity and stereotypical behavior, such as grooming abnormalities in both, social interaction and vocalizations, and increased anxiety. To create Shank2 brain specific KO mice, the Cre/loxP recombination system was used. Altogether, we analyze three different KO mouse models which display a loss of Shank2 either in all *CamK2a* (Calcium-dependent-protein-kinase-type2-alpha) -expressing cells constitutively or after treatment with Tamoxifen, a synthetic estrogen antagonist, or in neuronal subpopulations, e.g. in Adora2a-expressing cells of the indirect pathway of the dorsal striatum. Finally, we are interested in understanding different behavioral abnormalities involved in ASD and the underlying brain regions.



Steffen Halbgebauer

Born in 1987, I finished my bachelor's and master's degrees in Molecular Medicine at Ulm in 2011 and 2013, respectively. In October 2013, I started my PhD thesis at the Institute of Experimental Neurology under the supervision of Professor Dr. M. Otto. At the same time, I also joined the International Graduate School in Molecular Medicine.

Validation of neurochemical candidate markers for the early diagnosis of neurodegenerative diseases with special attention being paid to the differentiation of Parkinson's disease and Parkinson's disease dementia.

In my PhD thesis I am working on the discovery and validation of possible markers for an early detection of neurodegenerative diseases. Consequently, I especially focus on the differentiation of Parkinson's disease and Parkinson's disease dementia by examining human serum and cerebrospinal fluid with mostly mass spectrometric and isoelectric-focusing immunoassay approaches.

Stephanie Hampp (née Biber)

I was born in 1985 and started my PhD thesis in the laboratory of Prof. Dr. Lisa Wiesmüller at the Department of Obstetrics and Gynecology in 2012. After being financed the first year with a scholarship from the state of Baden-Württemberg, I started the PhD Programme in Molecular Medicine at the IGradU in 2013.

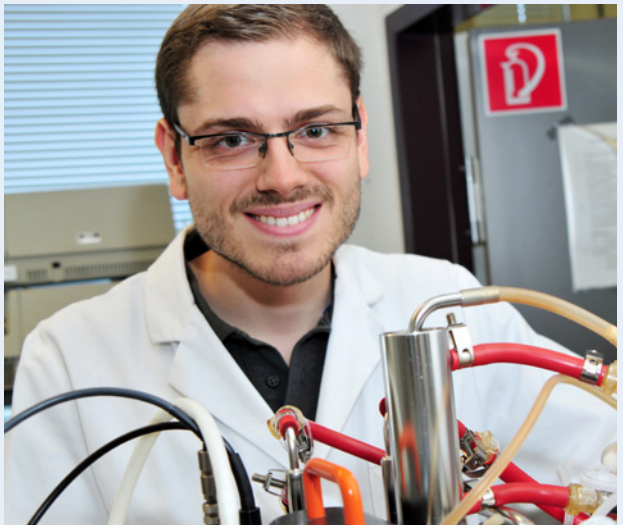
Regulatory role of 3`-5` exonuclease-active p53 in the reactivation of stalled replication forks

p53 possesses an intrinsic 3`-5` exonuclease activity located within its central DNA-binding domain.[1] However, the relevance of this activity has largely remained obscure. Its potential involvement in DNA repair has been attributed to transcription-independent functions of p53 in nucleotide and base excision repair (NER, BER, respectively) and in homologous recombination (HR).[2-4] In particular, the role of p53 regarding HR seems contradictory. On the one hand, it has been reported that p53 downregulates error-prone, unscheduled and excessive HR.[2-4] On the other hand, p53 stimulates HR to overcome DNA barriers, which may lead to replication fork stalling and, ultimately, fork collapse.[4-6] In this way, p53 should prevent tumorigenic genome rearrangements in response to severe genotoxic stress and protects replicating DNA under physiological conditions. As the mechanism, how p53 downregulates HR is well described in the literature I want to elucidate in my PhD thesis as well as how p53, as the molecular mechanism, stimulates HR during DNA synthesis and the impact of p53 exonuclease activity in this process.

1) Mummenbrauer et al. Cell 1996. 2) Bertrand et al. Trends Genet 2004. 3) Sengupta et al. Nat.Rev. Mol Cell 2005. 4) Gatz and Wiesmüller Cell Death Differ 2006. 5) Restle et al., Nucl Acid Res 2008/6: Ireno et al. 2014, Carcinogenesis.

Julia Harant

Born in 1991, she is working in the trauma lab of the Department of Orthopedic Trauma, Hand, Plastic and Reconstruction Surgery at the Center for Biomedical Research, which is included in the SFB 1149. She is a member of the group of Prof. Dr. med. Markus Huber-Lang and enrolled in the study program in Experimental Medicine. She started her study of Human Medicine in 2011 at Ulm University.



Markus Johannes Harder

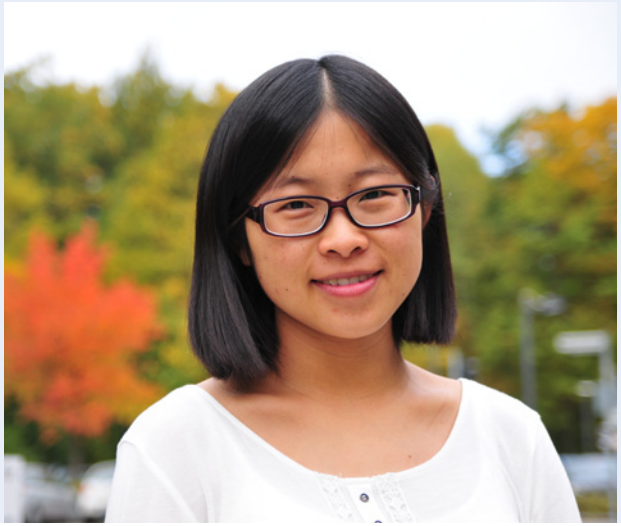
Born in 1987, he studied Chemistry and Biochemistry at the Ludwig Maximilian University of Munich and is currently working at the Institute of Clinical Pharmacology and Pharmacology of Natural Products. He has been participating at the International Graduate School in Molecular Medicine Ulm University since the winter semester of 2014/15.

Microvesicle-induced immune response after trauma

Nearly fifty per cent of patients suffering from traumatic injuries develop a systemic inflammatory response. The immune system is activated not only by exogenous pathogens but also by endogenous subcellular structures that lead to this inflammatory response. Furthermore, it has been shown that different cell types, even if they are not activated and completely intact, are able to shed microvesicles (MVs) from their outer layer of the plasma membrane. Several pretrials performed by the lab revealed the generation of C5a-receptor-positive MVs out of neutrophil granulocytes after stimulation with CRP. Therefore, it will be investigated to what extent MVs trigger the overwhelming immune response and the dysfunction of the complement and clotting system.
First, the trauma-induced shedding of MVs will be shown by collecting plasma samples from patients suffering a polytrauma with an injury severity score of more than 25 points. The blood samples are taken immediately and after 8, 24, 48, 120 and 240 hours. After centrifugation, the number of MVs is analyzed with flow cytometry by comparison with counting beads. The count of MVs will then be correlated with the severity of the trauma and the clinical outcome.
Second, the cellular origin of the MVs will be detected by using FITC and PE-conjugated anti-human-specific CDs for several cell types. In addition, it will be examined whether MVs bear clotting factors, such as tissue factor, or complement and toll-like receptors.

Natural and engineered complement regulators in health and disease

The involvement of the complement system in several inflammatory, immune and age-related diseases is increasingly recognized and has boosted interest in understanding in detail how complement is regulated.
The aim of my PhD project is to advance the understanding of physiological complement regulation by unmasking the structure-function relationship of crucial regulators within the Factor H protein family and by exploring the pathogenic role of certain mutations in these regulators. The gained knowledge is then exploited for the engineering of artificial complement inhibitors that outperform physiological complement regulators in terms of target specificity and regulatory activity. The therapeutic potential of these molecules will be tested in *ex vivo* assays and animal models of complement-mediated disorders such as e.g. Paroxysmal Nocturnal Hemoglobinurea, Atypical Hemolytic-Uremic Syndrome or Age-Related Macular Degeneration (in collaboration).
All in all, my project seeks to provide a structure-function toolkit for the rational engineering of potent inhibitors that are tailored to the clinical needs of different complement-mediated diseases.



Jiajia He

Born in 1988, I am from Nanjing, China. Since October 2014, I have worked as a PhD student at the Institute of Physiology Chemistry, Ulm University. We are interested in the effects of transcriptional factor FoxO3 in glucose metabolism regulation. My current PhD project focuses on the role of hepatic FoxO3 in the regulation of glucose metabolism.

Verena Heidler

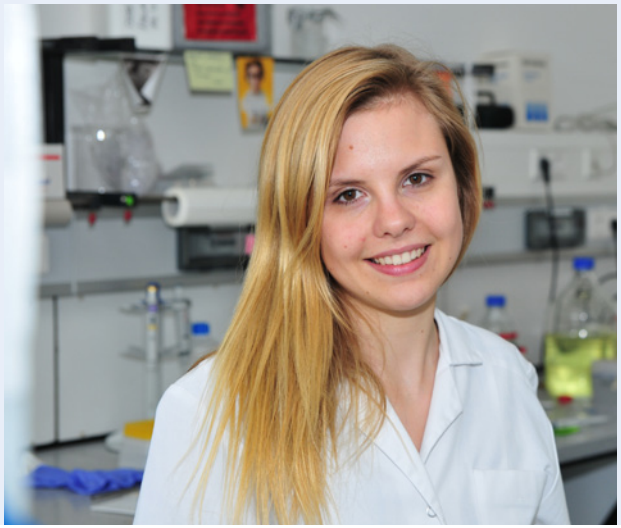
Born in 1988, she completed her bachelor's in Nutritional Science and her master's in Nutritional Medicine at the University of Hohenheim. She started her PhD program at the IGradU in April 2014. She is currently working at the Institute of Orthopedic Research and Biomechanics where she is investigating the effects of calcium and vitamin D on fracture healing and posttraumatic bone turnover.

The role of hepatic FoxO3 in the regulation of glucose metabolism

The liver plays an important role in glucose metabolism, both under physiological and pathological conditions. A typical pathological condition, where hepatic glucose metabolism is deregulated, is type 2 diabetes, for which excessive hepatic glucose production is a hallmark.
Among the many factors that are involved in the regulation of hepatic glucose metabolism, the FoxO family plays a prominent role. Mammals have four FoxO family members: FoxO1, FoxO3, FoxO4 and FoxO6. Up till now, the specific individual role of FoxO3 in hepatic glucose metabolism has been incompletely understood. In a previous study, it was shown that continuous active FoxO3 expression in hepatocytes *in vivo* at first leads to hyperglycemia and. later on, to severe hypoglycemia, hyperinsulinemia and pancreatic hyperplasia. These effects could be rescued by the administration of metformin. However, there were many open questions in regard to the development of this phenotype.
One important question is how activation of FoxO3 in the liver leads to hypoglycemia and pancreas hyperplasia. This could either be an excessive response to the preceding hyperglycemia, but it could also be due to specific liver-derived systemic factors, such as betatrophin, which is a matter of controversial debate.
The objectives of this study were to generate more data on the development of the phenotype, to explain how pancreatic hyperplasia comes about in mice with continuous FoxO3 expression, and to identify possible mechanisms of how metformin could interfere with FoxO3 function.

Effects of calcium and vitamin D on fracture healing and posttraumatic bone turnover

Osteoporosis is the most common skeletal disorder worldwide and is associated with increased fracture risk and disturbed fracture healing. Important osteoporosis risk factors with increasing age are calcium and vitamin D deficiencies because dietary intake, intestinal absorption and endogen synthesis are reduced. As calcium and vitamin D play key roles in bone metabolism, insufficient supply negatively affects bone properties and possibly the fracture healing process. However, studies investigating the effects of calcium and vitamin D on fracture healing are limited. Calcium is mandatory for callus mineralization and thus a sufficient supply seems to be necessary. Identification of the influence of calcium and vitamin D on fracture healing may have direct effects on clinical therapy of osteoporotic fractures and prevent posttraumatic bone loss. Indeed, clinical studies show that fractures lead to a loss of mineralized bone mass that also affects the intact skeleton and, thereby, further increases fracture risk.
Therefore, this project examines the effect of a calcium and vitamin D deficiency and supplementation on osteoporotic fracture healing and posttraumatic bone turnover. Due to the increasing prevalence of osteoporosis, this project is of high clinical relevance.



Anika Marie Helferich (née Bronnhuber)

Born in 1989, I studied the bachelor's degree course in Molecular Medicine at Ulm University, followed by the international master's course of studies in Molecular Medicine. After conducting my master's thesis at the Mayo Clinic in Jacksonville (Florida), I joined the working group of Prof. Dr. Jochen Weishaupt at the Department of Neurology of Ulm University for my PhD studies.

Estefania Herdoiza Padilla

Born in 1992 in Quito, Ecuador, Estefania is a PhD student at the Institute of Microbiology and Biotechnology, Ulm University, and holder of a PhD scholarship for the doctoral study course in Pharmaceutical Biotechnology (Kooperatives Promotionskolleg "Pharmazeutische Biotechnologie"). She is also part of the International PhD Programme in Molecular Medicine of Ulm University.

The generation and characterization of a new ALS mouse model for analyzing TDP-43 oligomerization *in vivo*

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by a progressive loss of the upper and lower motor neurons. As both motor neurons are involved in controlling and execution of voluntary movement, their degeneration leads to spasticity, paralysis and muscular atrophy. In 2006, the TAR DNA-binding protein 43 (TDP-43) was identified as a major component of ubiquitin-positive intracellular inclusions in affected brain regions of ALS patients (Neumann et al., 2006). Although several transgenic TDP-43 mouse models exist, none of these mouse models allow a quantification of the formation and spreading of TDP-43 oligomers and aggregates, and its meaning for neurodegeneration (Tsao et al., 2012). Thus, we want to generate a new transgenic mouse model which inducibly (Tet-off-system) co-expresses TDP-43 fused to the c-terminal fragment (TDP-43-V1) and TDP-43 fused to the n-terminal fragment of Venus-YFP (TDP-43-V2) in the forebrain. Upon interaction of TDP-43-V1 and –V2, the fluorescence of Venus-YFP is restored, representing a measure of TDP-43 oligomerization. In summary, the aims of my PhD project are to establish and then to characterize a new transgenic mouse model that allows the analysis of TDP-43 oligomerization *in vivo*.

miRNA-dependent regulation of phagocytosis

Phagocytosis is a complex process by which infected or dead cells, extracellular pathogens and foreign particles are ingested and removed from the circulation by phagocytes, in particular, macrophages. Depending on the cytokine microenvironment, macrophages can either be classically activated (pro-inflammatory M1 macrophages) or alternatively activated (anti-inflammatory M2 macrophages). After *ex vivo* differentiation from human blood monocytes, M1 and M2 macrophage subsets exhibit different surface markers, functions and phagocytic activity.
Non-coding miRNAs are a family of small RNA molecules that negatively regulate the expression of different target mRNAs in a sequence-specific manner. Abnormal miRNA expression has been associated with the development and progression of different human diseases such as cancer and immune-related diseases. The role of individual miRNAs in the normal development and the maturation of B cells as well as their function in the polarization of T cells have been well characterized. However, the influence of miRNA regulation on phenotype determination, phagocytic activity and apoptosis of macrophages is poorly understood.
The aim of this project is the identification of miRNAs that regulate phagocytosis and apoptosis in human M1 and M2 macrophages.

Tanja Hering

Born in 1986. After completing her intermediate diploma in Biology at the University of Ulm Karlsruhe (TH), she finished her diploma in Molecular Biology at Ulm University in 2011. Following her interest in medical research, she started her PhD at the IGradU at the Institute of Experimental Neurology under the supervision of Prof. Orth and completed it with her defense in June 2015.

Elisabeth Hermkes

Born in 1990 in Bautzen, she works at the Institute of Pharmacology and Toxicology at Ulm. She started her PhD in October 2013 in the International PhD Programme in Molecular Medicine. Her thesis is part of the DFG-funded Collaborative Research Center 1074 "Experimental Models and Clinical Translation in Leukemia." In her free time, she is engaged in the Student Initiative Association of Biotechnology (Biotechnologische Studenteninitiative e.V.).

Brain, skeletal muscle and liver mitochondrial biology in the R6/2 fragment model of Huntington's Disease (HD)

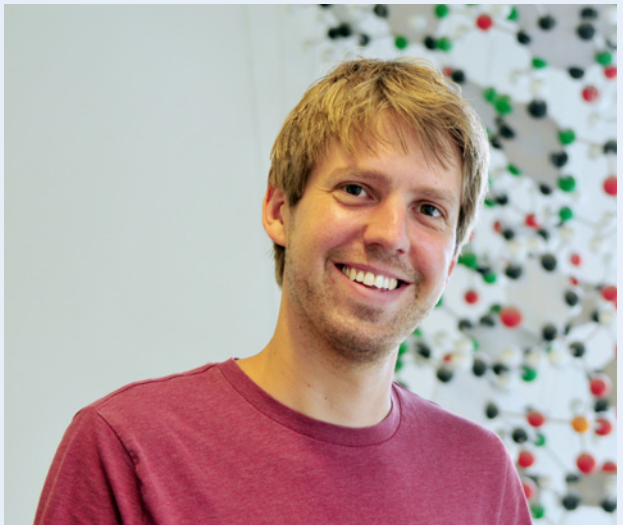
Brain, skeletal muscle and liver mitochondrial biology in the R6/2 fragment model of Huntington's Disease (HD) is a fatal autosomal-dominant neurodegenerative disorder caused by a CAG triplet repeat expansion mutation in the huntingtin (*HTT*) gene. *HTT* is expressed ubiquitously and affects predominantly, but not exclusively, striatum and cortex. The function of normal and mutant HTT (mHTT) is still not completely understood, but it has been shown to influence several organelles including mitochondria. Different aspects of mitochondrial biology are affected by mHTT. However, the findings of mitochondrial alterations in HD are very heterogeneous. This might be caused by the different HD disease stages, HD model, cell lines and tissues that have been used to assess mitochondrial biology in HD. Mitochondrial shape, proteomic composition and functional priorities vary between tissues. To untie the mitochondrial biology in HD according to commonalities and tissue-specific differences, we investigated in a comparative and comprehensive study the mitochondrial biology in different tissues from one HD model. Different aspects of mitochondrial biology, including morphology, fission and fusion balance, biogenesis, mitochondrial respiratory chain assembly and function in striatum, cortex and whole brain, together with muscle and liver, were assessed in the R6/2 HD fragment mouse model.

Functional analysis of the Rho GTPase/phospholipase C-γ_2 interaction in chronic lymphocytic leukemia

The physiology of normal B cells is tightly controlled by the B cell antigen receptor (BCR) and associated signal transduction proteins, including inositol-phospholipid-metabolizing enzymes such as phospholipase C-γ_2 (PLCγ_2). Functional and/or structural alterations of these signaling proteins disrupt the homeostatic balance between programmed cell death and survival as well as between proliferation and differentiation of B cells, resulting in B cell lymphoid malignancies such as chronic lymphocytic leukemia (CLL). Bruton's tyrosine kinase (Btk) is a central player in BCR signaling through its ability to activate PLCγ_2. It is therefore essential for the survival of CLL cells and their homing to microenvironmental niches. Several small molecule Btk inhibitors were developed as a new class of targeted agents for the treatment of CLL, showing impressive clinical efficacy in relapsed/refractory CLL. Ibrutinib, the most advanced compound of this class, irreversibly inhibits Btk protein kinase activity, resulting in decreased CLL cell proliferation and survival as well as homing to and retention in tissue microenvironments. In some cases, however, acquired resistance to ibrutinib limits its therapeutic efficacy. Mutations in the *PLCG2* gene were identified in patients with acquired resistance to ibrutinib. The aim of the project is to understand the functional consequences of these mutations and to identify the mechanisms of *PLCG2*-mediated ibrutinib resistance at the molecular and cellular level.

Julia Katharina Herzig

Born in the eighties.
I am working on my PhD studies at the Department of Internal Medicine III, Ulm University Medical Center. In the research group of Prof. Döhner, we decipher the molecular biology of acute myeloid leukemia.
At the beginning of my PhD two years ago, I joined the PhD program of the International Graduate School in Molecular Medicine.



Raphael Hesse

Born in 1987 in Tettnang. I am currently working on my PhD thesis at the Department of Experimental Neurology. I studied Biology at the Karlsruhe Institute of Technology (KIT) and completed my diploma thesis at the Institute of Cell and Neurobiology. I am pursuing my PhD at the International Graduate School in Molecular Medicine Ulm.

Functional analysis of recurrent deletion of chromosomal band 3p14.1-p13 in acute myeloid leukemia

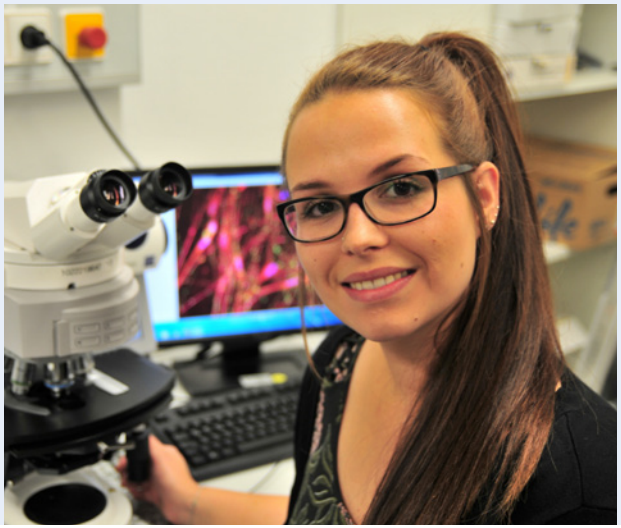
Acute myeloid leukemia (AML) is a clonal neoplastic disease of the hematopoietic system that is characterized by its enormous clinical as well as genetic heterogeneity. The identification of chromosomal alterations and gene mutations has elucidated the genetic basis of leukemia. An increasing number of these genetic abnormalities already have prognostic and predictive relevance, and these are used for risk-adapted therapy in the clinic. Nevertheless, a certain amount of genes involved in leukemia and their contribution to molecular pathogenesis of AML is still unknown. Using genome-wide single nucleotide polymorphism analyses, we recently identified a commonly deleted region (CDR) in chromosomal band 3p14.1-p13 in AML patients with normal karyotype. This CDR is about 2MB in size and consists of eight protein coding genes and one microRNA. This region is supposed to harbor putative tumor suppressor genes and we assume that the affected genes are potentially related to the molecular pathogenesis of AML.
Within this project, we aim to: 1) characterize the CDR by validation in additional AML patient cases; 2) perform mutation and epigenetic screening of the commonly deleted genes; and 3) investigate the candidate genes by functional analyses. Finally, we will correlate validated candidate genes with clinical characteristics and outcome to evaluate their prognostic and predictive relevance.

Effects of sAPPα and sAPPβ on morphology and function of primary hippocampal neurons

In patients with Alzheimer's disease (AD), cerebral metabolism of amyloid precursor protein (APP) is altered by affecting Amyloid-β (Aβ) and potentially sAPPα and/or sAPPβ levels. Cognitive impairments in AD patients are associated with synapse loss and loss in brain volume. Long-Term-Potentiation (LTP), the cellular basis of learning, is impaired in several AD model systems. These impairments are thought to be a consequence of the disturbed cerebral APP metabolism, forcing an extensive overproduction of Aβ peptides. Aβ peptides are produced by a sequential cleavage of APP. APP is metabolized by two distinct pathways. It is first cleaved by either an α-secretase (non-amyloidogenic) or a β-secretase (amyloidogenic) and a subsequent γ-secretase cleavage. Within the non-amyloidogenic pathway, sAPPα (soluble APP α) is generated, whereas via the amyloidogenic pathway, sAPPβ (soluble APP β) and the Aβ peptides are produced. As a consequence of the shift towards the β-secretase-cleavage in AD patients, not only are Amyloid-β peptides overproduced, but also less sAPPα is generated. This may be of particular interest in AD pathogenesis since sAPPα is known to have neurotrophic properties. Only a few studies on sAPPβ exist. Therefore, I investigate the molecular mechanisms of sAPPα and sAPPβ actions on primary hippocampal neurons in a head-to-head comparison.

Elena Heusinger

Born in 1991, she started her studies in Biology at the University of Hohenheim in 2010. In 2013, she came to Ulm University to study for a master's in Molecular Medicine. After the completion of her master's thesis at the Institute of Molecular Virology, she continued her PhD studies at the same institute as part of the International Graduate School in Molecular Medicine.



Julia Higelin

I was born in December 1988 and started my studies in Biology in 2009 at Ulm University. I joined the International Graduate School in Molecular Medicine Ulm in April 2015 after I had received my master's degree in Biology. I am currently a PhD student at the Institute for Anatomy and Cell Biology under the supervision of Prof. T. Boeckers and Dr. Maria Demestre.

Molecular mechanisms and evolution of antiretroviral host proteins

Viruses and their hosts are in a continuous arms race. As a measure against viral infections, host cells have developed so-called restriction factors, which inhibit viral replication. In turn, viruses have also evolved in order to escape those restrictions. In this scenario, viruses and hosts influence the evolution of each other. It is, therefore, of interest to elucidate the evolutionary origins of antiviral host proteins as well as their mode of action in order to understand the role of these proteins in the evolution of viruses.

One particularly interesting host restriction factor is tetherin, a protein that inhibits the release of a broad variety of enveloped viruses. In contrast to some other restriction factors, tetherin is a very ancient protein that evolved early during vertebrate evolution and has therefore probably influenced the evolution of many viruses (Heusinger et al., 2015).

Notably, it has been shown that tetherin constitutes a major barrier for the rise of the HIV-1 pandemic as tetherin counteraction is a critical step for the spreading of lentiviruses in the human population. Yet, the role of tetherin during the emergence of HIV-2 or zoonotic transmissions of influenza viruses is less clear. My PhD project therefore focuses on the adaptation of HIV-2 and influenza viruses to the tetherin orthologs of different host species. The results of this work will increase our understanding of the factors that determine efficient cross-species transmissions of viruses from one host to another.

Characterization and motoneuronal differentiation of human (ALS-) induced pluripotent stem cells

Amyotrophic lateral sclerosis (ALS) is characterized by the degeneration of upper and lower motoneurons (MN) and leads to death due to respiratory failure. In 5% of familial ALS (fALS) cases, mutations in FUS (Fused in Sarcoma) have been identified as a genetic cause of the disease. FUS is a RNA-binding protein and is involved in many processes of gene expression. In addition to its predominant localization in nucleus, FUS is also detectable in synaptic spines and dendrites in neurons.

ALS-related FUS mutations are clustered in the nuclear localization signal (NLS). This leads to an abnormal distribution between nucleus and cytoplasm. Furthermore, in the brain and spinal cord of an affected patient, FUS is found in cytoplasmic inclusions.

On the basis of human-induced pluripotent stem cells (hiPSCs), we are able to differentiate MNs from healthy controls and fALS-FUS patients. Based on the putative role of FUS in mechanisms related to plasticity and local rearrangement of synaptic contacts, we want to investigate FUS with respect to its localization in MNs derived from patients and controls. The thesis is also focused on the comparison of iPSCs and MNs with respect to cell differentiation, morphology and protein expression under physiological and stress conditions. To avoid individual differences due to genetic background, we want to generate isogenic controls by the CRISPR/Cas9 system. In this way, we hope to identify factors which lead to pathological protein aggregation and, thereby, to clarify neurodegeneration.

Lisa Hipp

Born in 1988 in Esslingen, I started my bachelor's studies in Molecular Medicine in 2008 at Ulm University. My subsequent master's studies in Biochemistry aroused my interest in Biophysics. Hence I joined the IGradU in November 2014 to participate in a cooperative PhD project at the Institute of Physiological Chemistry in the work group of Prof. Dr. Knöll and at the Institute of Biophysics (Prof. Dr. Michaelis).

Susanne Hirsch

I was born in 1990 and, in 2009, I joined the study program of Molecular Medicine at Ulm University. In the course of my doctorate, I am working in Prof. Bullinger's team in the Department of Internal Medicine III.
I have always had a passion for traveling and, as a scientist, have had the opportunity to meet interesting people from all over the world and to learn more about their cultures and countries.

Analyzing the impact of nuclear architecture on neuronal gene regulation by high resolution imaging techniques

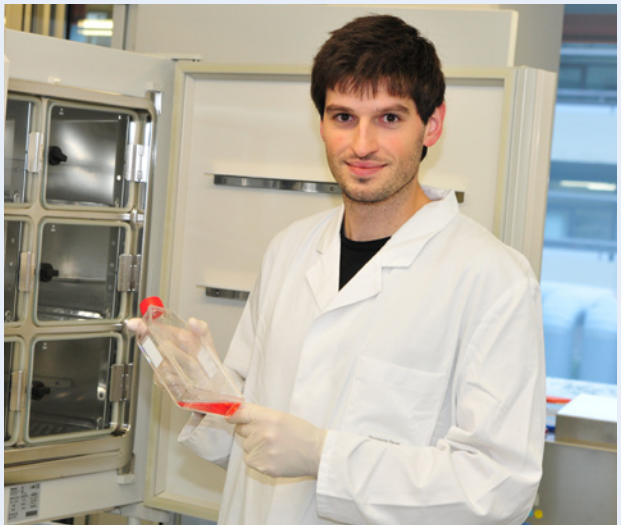
The regulation of gene expression is crucial for the adaptability and versatility of all organisms and depends on the fine-tuned interplay of epigenetic modifications, transcription factors and, as recently shown, changes in nuclear architecture. We are especially interested in the transcription factor serum response factor (SRF), which fulfills numerous important roles in the developing and adult brain. By using high resolution microscopy such as Stochastic Optical Reconstruction Microscopy (STORM), we investigate interactions of SRF with both target genes and partner proteins after an external stimulus in the three-dimensional nuclear environment of neuronal cells. In a live-cell approach, we are moreover examining possible changes in the binding dynamics of SRF after stimulation.
A second project deals with the formation of filamentous actin networks in the nucleus. Although many publications confirm the existence of nuclear F-actin structures, there is still little known about possible functions. We are planning to visualize different filamentous actin structures in the nuclei of neurons with the highest possible resolution by using electron microscopy and high resolution fluorescence microscopy.

Characterization of pathogenetically relevant circular RNAs in acute myeloid leukemia (AML)

In the pathogenesis of acute myeloid leukemia, both mutations in genes regulating the splicing process and non-coding RNAs have been shown to play an important role. We aim to investigate the newly discovered class of non-coding RNAs termed circular RNAs in the context of AML. circRNAs are abundant, conserved and their expression is specifically regulated.
We will identify AML-associated circRNAs via the evaluation of the whole circular transcriptome of AML patients by performing RNA-seq with data sets treated with RNase R. circRNA expression will be correlated with clinical and cytogenetic data and mRNA expression profiles.
To examine circRNA functions and their influence on differentiation, we will synthesize circRNAs *in vitro* and transfect AML blasts with "mature" circRNAs. A converse approach will be the specific siRNA-mediated knockdown of a circRNA. Using our overexpression and knockdown systems, we will characterize the morphology and differentiation status of the cells, conduct cell proliferation and apoptosis assays, and perform gene expression profiling.
An affinity pull-down assay of biotinylated circRNA will enable identification of circRNA interacting nucleic acids and proteins via sequencing and mass spectrometry.
Altogether, characterization of circRNA expression and function in hematopoietic disorders will lead to a better understanding of AML biology and might improve AML diagnosis, prognosis and therapy.

Sofia Hirth

Born in 1986. I am a student of the International PhD Programme in Molecular Medicine and a member of the Department of Internal Medicine II (Molecular Cardiology). Our lab is mainly focusing on the genetic and molecular networks of heart development and function. The long-term goal of our research is the development of new therapies for heart/ muscle diseases.



Daniel Hochdorfer

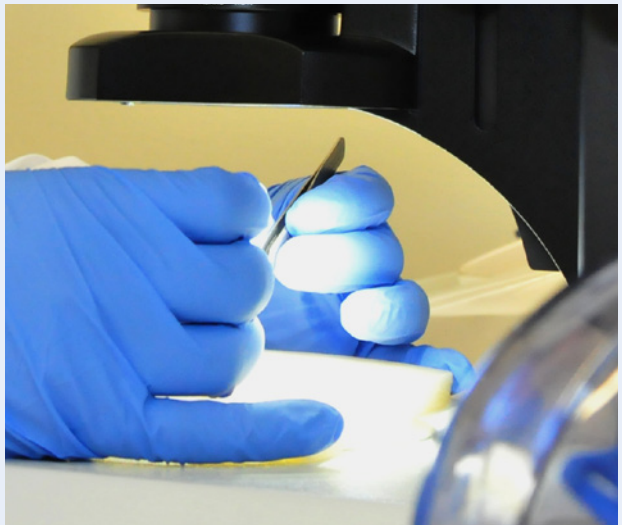
Born in 1987, I joined the group of Prof. Christian Sinzger at the Institute of Virology in 2012 for my diploma thesis and afterwards stayed to complete my PhD thesis. In 2013, I joined the International Graduate School in Molecular Medicine Ulm as an associate member of its PhD program.

Paxillin-FAK protein complex as an essential regulator of cardiac contractility in the zebrafish heart

The Integrin-linked Kinase (ILK) is an important part of the cardiac stretch sensor and was found to be mutated in patients suffering from dilated cardiomyopathy. In the search for key regulators of cardiac contractility, we isolated the zebrafish mutant *main squeeze (msq)*. *Msq* mutant embryos display progressive heart failure due to a mutation within the *ilk* gene. Together with Pinch and Parvin, ILK forms the ILK-Parvin-Pinch (IPP) complex. It was shown that the IPP-complex controls cardiac contractility via Protein Kinase B (PKB) signaling in zebrafish. To further elucidate the underlying molecular mechanisms of mechanosensing in cardiomyocytes, we investigated other known interaction partners of the IPP complex. Paxillin interacts with the IPP complex by binding to β-Parvin and ILK. We showed that depletion of Paxillin results in a progressive decrease of cardiac contractility in zebrafish embryos without affecting IPP-PKB signaling. However, we found that Paxillin deficiency leads to the destabilization of its binding partner FAK. Vice versa, inactivation of FAK results in the degradation of Paxillin proteins and subsequent contractile dysfunction. Interestingly, knockdown of either FAK or Paxillin leads to degradation of Vinculin, which is known to play an essential role in mechanosensing. These findings highlight a crucial role of the Paxillin/FAK complex in controlling cardiac contractility via its interaction with Vinculin, independent of IPP-PKB signaling.

Host factors contributing to initial events of HCMV infection

The group of Prof. Christian Sinzger focuses on the entry of the human cytomegalovirus (HCMV) into host cells. Endothelial cells are considered to have a pivotal function in hematogenous dissemination and viral spread during HCMV infection. Although several cellular proteins have individually been reported as putative viral receptors, none of them has been confirmed in endothelial cells. The aim of my study is to identify and characterize host factors contributing to initial events of HCMV infection in endothelial cells. Host factors that promote HCMV infection would be candidate entry receptors for HCMV. I address this by an RNA interference high-throughput assay to identify cellular host factors that affect HCMV entry into endothelial cells. The siRNA library used in this screen targets candidates from promising molecule classes such as integrins, chemokine receptors, growth factor receptors, adhesion molecules, immunoglobulin superfamily and tetraspanins. Host factors that promote infection, as identified in the screen, are then further characterized regarding their mode of action. This work aims at advancing the knowledge of the so far incompletely understood entry process of HCMV.



Felix Hönes

Born in 1989, he studied Medicine at the Goethe University of Frankfurt from 2010 to 2012 and has been studying at Ulm University since 2012. He now conducts research in the Traumalab in the Department of Orthopedic Trauma, Hand, Plastic and Reconstructive Surgery, Ulm University Hospital.

Maria Hollnagel

I was born in 1986 in Chemnitz. My intrinsic curiosity in wishing to understand the use of biological elements on the brain led to my studies in Psychology (Chemnitz) and Biochemistry (Magdeburg). Besides science, I am an avid fan and player of volleyball, which I have played up to the second German league. Currently, I am prioritizing my PhD thesis which I am completing in Ulm at the Institute of Experimental Cancer Research.

Trauma-induced barrier dysfunction

Polytrauma is one of the leading causes of death among young people. Most common subsequent complications are systemic in‹ammation and multiple organ dysfunction and failure that are accompanied by high mortality. Current reports suggest that these circumstances are associated with development of an occult or manifest blood-organ dysfunction.
The aim is to identify new markers which allow the detection of barrier breakdown. First results of the research gruop around Prof. Huber-Lang indicate that some tight-junction molecules can be detected in the circulation of patients after severe tissue injury. These proteins will therefore be analyzed in polytrauma patients treated at the Department of Orthopedic Trauma (Prof. Gebhard) and will be related to clinical data. In addition to this, a cell model of the blood-organ-barrier should expand the investigation of the release of barrier molecules into the circulation and could serve as a marker for monitoring the immune function and specific organ performance in a patient after injury.

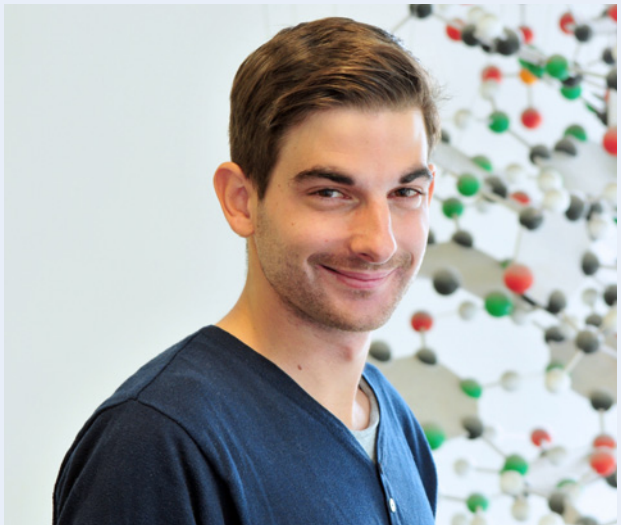
Role of PHF19 in normal and leukemic hematopoiesis

Leukemia is still a deadly disease in which malignant cells compete with healthy cells. Despite chemotherapy and bone marrow transplants, up to eight out of ten patients currently die due to acute myeloid leukemia. New therapies are in high demand in order to increase the cure rate. To understand the biology of the disease, both the different gene-expression patterns of molecular regulators in leukemic cells and the mechanisms involved in the misregulation of molecular regulators during hematopoiesis are analyzed. It is known that epigenetic mechanisms regulate normal hematopoiesis and that abnormal regulations can lead to leukemia. The term “epigenetics” describes stable alterations of DNA, which are heritable but do not involve mutations of the DNA itself. This is achieved by adding “molecular flags” on DNA or on DNA-packaging proteins. These “flags” are recognized by other proteins and this leads to a cascade of molecular processes.
PHF19 is one such “flag reader.” It recruits other protein complexes to specific regions of the DNA upon which gene silencing occurs in murine stem cells. However, the role of PHF19 in normal hematopoiesis and acute myeloid leukemia (AML) is not known. In normal hematopoiesis, stem cells self-renew and differentiate to give rise to mature cells. It will be interesting to see to what extent PHF19 is involved in such cell processes. Therefore, *in vitro* colony-forming cell and proliferation assays with human and murine bone marrow, as well as *in vivo* murine bone marrow transplantation assays, are part of my work.

priv.

Dominik Hotter

Born in 1988 in Füssen, Germany, he obtained his bachelor's and master's degrees in Molecular Medicine at Ulm University. He is currently doing his PhD studies with funding from the International Graduate School in Molecular Medicine Ulm at the Institute of Molecular Virology under the supervision of Prof. Frank Kirchhoff.



André Michael Huss

Born on 11 January 1987 in Ehingen, Donau, I completed my BSc and MSc degrees in Biology at Ulm University in 2010 and 2012, respectively. Since 2013, I have been participating in the PhD program of the International Graduate School in Molecular Medicine Ulm under the supervision of Prof. Dr. M. Otto and Prof. Dr. H. Tumani (Department of Experimental Neurology).

Differential regulation of NF-κB-mediated proviral and antiviral host gene expression by primate lentiviruses

The transcription factor NF-κB plays a dual role during lentiviral infection. On the one hand, NF-κB is a key regulator of the antiviral immune response, while on the other hand, it is exploited by lentiviruses, such as HIV-1, to ensure efficient viral transcription. These opposing roles of NF-κB on virus transcription and innate immune responses make it necessary for primate lentiviruses to tightly regulate its activation.

We have shown that the accessory protein Nef, which is expressed early during lentiviral infection, enhances NF-κB activation to ensure efficient transcription of viral genes, while Vpu, another accessory protein which is expressed at later stages of infection, blocks NF-κB activation to limit the expression of antiviral genes.

The *vpu* gene, however, was acquired rather late during lentiviral evolution in the lineage of simian immunodeficiency viruses that gave rise to HIV-1 after cross-species transmission to humans. This raises the question of how other primate lentiviruses that do not express Vpu inhibit NF-κB-induced antiviral immune responses. We are currently investigating the contribution of the accessory viral protein R (Vpr), which is expressed by all primate lentiviruses, to the control of NF-κB activation and also whether Nef-mediated downmodulation of the CD3 T-cell receptor by viruses that do not express Vpu can limit the induction of antiviral immunity.

Prospective multi-center validation and proteomic discovery of candidate protein biomarkers in cerebrospinal fluid

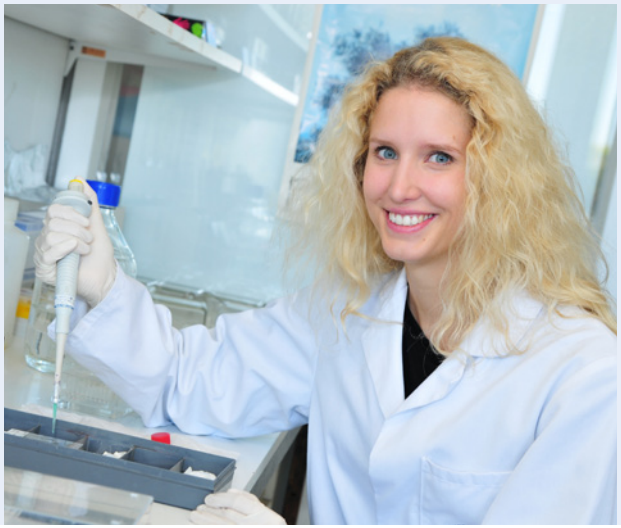
My PhD thesis aims at the validation of known potential biomarkers in multiple sclerosis (MS) as well as discovering new promising candidate biomarkers. Therefore, on the one hand, the so called MRZ reaction (detection of intrathecal-produced antibodies against measles, rubella and varicella zoster), the chemokine CXCL13, neurofilaments light chain (NfL) and Glial fibrillary acidic protein (GFAP) are validated in a prospective multicenter study by evaluating the correlation between the observed biomarker levels and patterns, and diagnosis and disease progression. The biomarker levels are determined in cerebrospinal fluid (CSF) and serum.

On the other hand, new biomarker candidates, especially to predict disease progression, will be identified using a proteomic approach which allows the detection of differentially expressed proteins in the CSF of different MS subtypes.

This project is taking place in cooperation with the Multiple Sclerosis Competence Network (KKNMS) in Germany.

Chiara Ianes

Born in 1990 in Trento, Italy. I began my studies in Biomolecular Sciences and Technologies at the University of Trento and continued my master's studies in Molecular Medicine at Ulm University. I started my PhD thesis under the supervision of Prof. Dr. Knippschild in the Department of General and Visceral Surgery (Ulm University Hospital) and also joined the international graduate program in 2015.



Daniela Jäger

Born in 1991, I am in the sixth semester of my studies in Medicine and now working on my doctoral thesis at the Institute of Pathology.

Characterization and effects of CK1-specific inhibitors on proliferation of pancreatic tumor cells and induced tumors in animal models

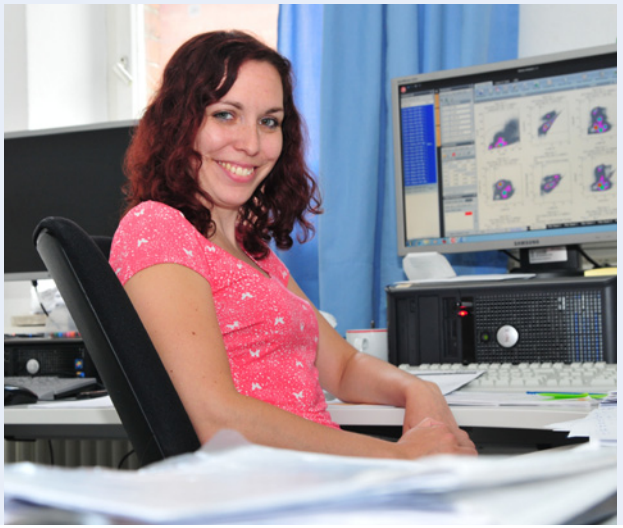
Pancreatic cancer is the fourth leading cause of death due to cancer worldwide. It is characterized by a high aggressiveness and a poor prognosis. Additionally, no early diagnosis and no effective cure are known so far. Therefore, it is relevant to further investigate both new and potential diagnostic marker and therapeutic agents. In this regard, the CK1 Ser/Thr protein kinase family seems to be a potential therapeutic target of inhibition, since its deregulation has been observed in different types of proliferative diseases, among which is pancreatic cancer. In fact, CK1 protein kinases are involved in the regulation of various important cellular processes (including DNA repair, proliferation, cytoskeleton dynamics, vesicular trafficking, apoptosis, and cell differentiation) which may be significantly affected in pancreatic cancer, once CK1 activity and/or expression is altered. Due to this consideration, my PhD thesis will focus on the screening of small-molecule CK1 inhibitors and on the further characterization of their effects on cell viability and cellular biology of pancreatic cancer cells, as well as their efficacy in pancreatic tumors of mouse models.

Molecular analysis of the clivus chordoma cell line U-CH 14 in comparison with eight sacral chordoma cell lines

Chordomas are rare, slow-growing bone tumors that are thought to originate from notochordal remnants. They arise along the spine and predominantly at the sacral region although rarely at the clival region. There is no efficient standard chemotherapy and the therapy of choice is surgery followed by radiotherapy. Chordoma recurs in up to 50% of patients and metastasizes in up to 40%. The chordoma cell line U-CH14 is worldwide the first cell line derived from clivus chordoma. My thesis focuses on the differences between clivus and sacrum chordoma, and the factors which determine their development at the different regions of the spine.
Therefore, I am conducting protein analyses of U-CH14 and two additional clivus chordoma cell lines using immunohistochemistry and western blot.
Furthermore, I intend to compare mRNA-expression of the different cell lines. As pretests have shown an activation of the CDK4/CDK6 pathway in chordoma and the effectiveness of the CDK4-inhibitor palbociclib, I intend to continue inhibition experiments by using palbociclib, abemaciclib and LEE011.

Christopher Jahn

Born in 1988, he received a BSc degree in Applied Biology from Bonn-Rhein-Sieg University and a BSc (Hons) degree in Bioscience and Biomedical Science from Robert Gordon University (Scotland). He earned his MSc degree in Molecular Medicine from Ulm University and joined the PhD program in 2013. He is supervised by Prof. Dr Gilbert Weidinger from the Institute of Biochemistry and Molecular Biology.



Sandra Jäkle

Born in 1987 in Konstanz, Germany. Since February 2015, I have worked in the Department of Otorhinolaryngology (Head and Neck Surgery) at Ulm University Medical Center. My PhD thesis focuses on adenosine-producing regulatory cell populations in patients with head and neck cancer. The results will help to improve current immunotherapeutic treatment approaches.

Tissue-specific functions of molecular signal transduction pathways during zebrafish fin regeneration

In contrast to mammals, some fish have the remarkable ability to regenerate their appendages after amputation. The cellular and molecular mechanisms behind this fascinating process are beginning to emerge, including substantial progress in the identification of signals that control regenerative growth of the zebrafish tail fin. Despite the rather simple architecture of the fin, the regulation of its regeneration is complex. Many signals, including fibroblast growth factor (FGF), Wnt, Hedgehog (Hh), retinoic acid (RA), Notch, bone morphogenic protein (BMP), activin, and insulin-like growth factor (IGF), are required for regeneration. In my research project, I am using the TetON system to induce tissue-specific conditional gene expression and, thereby, manipulate pathway function. With this powerful genetic tool, I aim to dissect tissue-specific functions of signaling pathways and how they interact during fin regeneration.

Adenosine (ADO)-producing regulatory cells in patients with head and neck squamous cell carcinoma (HNSCC) and their relevance for immunotherapeutic treatment

HNSCC belong to the most aggressive cancers in humans. The five year survival rate for advanced cancers is less than 50%. Recently, it has been shown that regulatory T cells (Treg) are positive for the ectonucleotidase CD39. CD39 hydrolyzes exogenous ATP to 5'-AMP. The enzyme CD73 hydrolyzes 5'-AMP to ADO, which is very immunosuppressive. Another cell population, which strongly expresses both enzymes, CD39 and CD73, are regulatory B cells (Breg). Immunosuppressive cell populations have a crucial influence on tumor development and metastasis. We therefore aim to characterize in detail ADO-producing B and T lymphocytes in patient blood as well as primary and secondary tumor sites.

One key enzyme for the function of immunocompetent B cells and Breg is the Bruton's tyrosine kinase (Btk). The mutation of Btk causes clinically relevant x-linked agammaglobulinemia. Our preliminary data suggest that ADO production in Breg is Btk-dependent. We will, therefore, compare the Btk expression of B cells of HNSCC patients before and after treatment with healthy controls to determine whether an active Btk influences tumor growth and metastasis.

The methods applied will include flow cytometry, luminescence for ATP metabolization, mass spectrometry, PCR and immunohistochemistry.

These analyses will strongly improve our understanding of tumor-induced tumor suppression and possible therapeutic consequences.

Simone Joas

I studied Biology at the University of Tübingen and gained my diploma degree in 2013. Since August 2013, I have been a member of the Research Training Group, CEMMA, as part of the International PhD Programme in Molecular Medicine. I am working at the Institute of Molecular Virology at Ulm University under the supervision of Prof. Dr. Frank Kirchhoff.

Kathrin Kaiser

Born in 1990, she studied Veterinary Medicine in Munich and finished her final exams in March 2015. In April 2015, Kathrin started working at the Institute of Orthopedic Research and Biomechanics. She focuses on the influence of the immune system on fracture healing after a severe trauma.

Increased susceptibility of CD4+ T cells from elderly individuals to HIV-1 infection and apoptosis is associated with reduced CD4 and enhanced CXCR4 and FAS surface expression levels

Elderly HIV-1 infected individuals show a more rapid loss of CD4+ T cells and progress more frequently to the acquired immunodeficiency syndrome (AIDS) than patients infected at a younger age. Additionally, HIV infection induces an accelerated aging of the immune system and many non-AIDS but age-related illnesses (hepatic, pulmonary, cardiovascular and renal disease, diabetes mellitus, dementia, arthritis) are more frequent in HIV-1-infected individuals than in age-matched uninfected people. HIV infection and aging share many characteristics since both are associated with a low production of naïve T cells, diminished T cell functionality, an accumulation of aging T cells, a loss of regenerative capacity and an increase of memory CD4+ T cells, which are predominantly infected by HIV and serve as a major cellular reservoir.
Thus, age is an important factor in AIDS progression because the regenerative capacity of people becoming infected at an older age is already reduced. To identify possible reasons for the differences in clinical progression, I perform comprehensive phenotypic analyses of CD4+ T cells from uninfected young and elderly healthy donors, and examine their susceptibility to HIV-1 infection and programmed cell death.

Mechanisms of interleukin-6 action in trauma-induced impairment of bone regeneration

More than 30% of patients with multiple injuries are additionally affected by fractures. These patients have a higher risk of delayed fracture healing or even non-unions. Our institute recently demonstrated in a rodent model that a severe trauma inducing an acute systemic inflammation causes delayed fracture healing. The additional trauma leads to a strong systemic activation of the coagulation and complement cascades and to the release of pro-inflammatory cytokines, but the underlying molecular mechanisms have not yet been exactly elucidated.
Here, we focus on the role of interleukin-6 (IL-6) which is not only a key cytokine in posttraumatic inflammation and pivotal for acute phase inflammatory responses and lymphocyte stimulation, but also mediates anti-inflammatory effects. We aim to investigate the role of the two different IL-6 signaling pathways. Whereas IL-6 trans-signaling using the soluble IL-6 receptor is considered as a danger signal and seems to act pro-inflammatory, classic signaling via the membrane anchored IL-6 receptor apparently promotes anti-inflammatory effects. Here, we will investigate the effect of trans-signaling in the pathomechanisms of compromised fracture healing induced by an additional severe trauma. The results of this study will help to develop novel therapeutic approaches to improve bone healing in severely injured patients. This study has a strong translational aspect because modulators of IL-6 pathways are already in clinical trials for other inflammatory diseases.

Naseebullah Kakar

Born in Pakistan in 1983. He completed his MSc at the University of Balochistan, Pakistan, in 2004 and his MS in Biotechnology and Informatics at BUITEMS, Pakistan, in 2009. Mr. Kakar was working as an assistant professor in the Department of Biotechnology, BUITEMS, Pakistan, before he joined the PhD program of the IgradU in 2012 in the lab of Prof. Kubisch and Prof. Borck at the Institute of Human Genetics.

Identification of genes responsible for autosomal recessive monogenic disorders in the Pakistani population: from candidate gene analysis to next generation sequencing

The overall aim of my thesis is to identify new disease-associated genes in a cohort of consanguineous families originating from Pakistan. In clinical genetics, the higher rate of consanguinity in the case of recessive diseases is creating a run of homozygosity containing the disease-causing genes, which is relatively convenient to find by adopting a particular approach, that is, from candidate gene analysis to next generation sequencing. Therefore, this approach offers the opportunity to identify new disease genes and to study the underlying genetic and pathophysiological mechanisms of monogenic diseases. The comprehensive aims of my thesis are to identify the underlying genetic cause of recessive monogenic diseases with the aim of identifying novel mutations , which expand the allelic heterogeneity, and are associated with phenotypes that significantly expand the genetic and phenotypic spectrum of the diseases. In addition, I aim to identify new disease-associated genes in a cohort of consanguineous families originating from Pakistan using genomic technologies and, also, to elucidate the molecular basis for the study of the molecular pathophysiology of diseases.

Stephanie Kallert

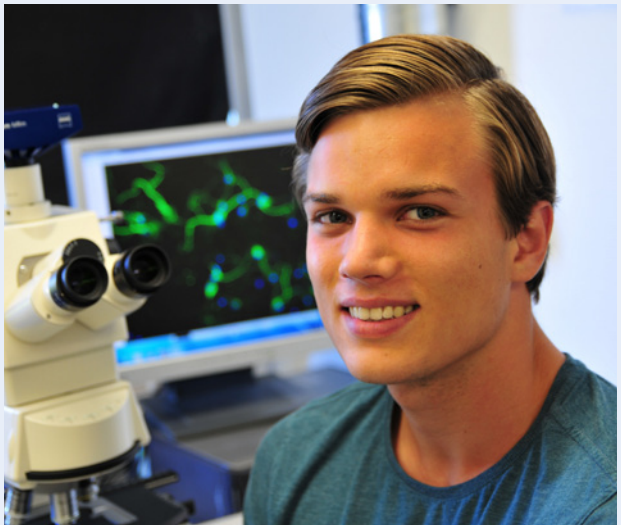
Born in 1987, she studied Biochemistry at the University of Tübingen. Between 2012 and 2015, she did her PhD at the Institute of Medical Microbiology and Hygiene in the "MyTB-Lab" (PI Prof. Dr. Steffen Stenger). "MyTB-Lab" focuses on understanding host pathogen interactions in human tuberculosis. The key objective is to develop novel vaccination strategies against tuberculosis.

Design and evaluation of strategies to optimize lipid-specific T-cell responses against *Mycobacterium tuberculosis (Mtb)*

Tuberculosis is one of the most frequent and deadly infectious diseases, and represents a major health problem worldwide. The most efficient way to prevent the spread of tuberculosis and to reduce the burden of disease worldwide is the development of an effective vaccine. The mycobacterial envelope represents an abundant source for lipid antigens which are increasingly acknowledged as new candidate antigens for vaccines.
This project has focused on improving the delivery of glycolipid antigens into human antigen presenting cells. The hypothesis was that delivery of the lipid antigen, lipoarabinomannan (LAM), via liposomes will promote the activation of T-cells. Liposomes containing lipoarabinomannan (LIPLAM) were prepared and characterized. The uptake of those liposomes in different cell types was analyzed and the biological activity of LAM was demonstrated by down-regulation of peroxisome proliferator-activated receptor gamma protein expression. Stimulation of primary human T-cells with LIPLAM induced a stronger IFNg secretion as compared to purified LAM and showed that delivery of glycolipid antigens via liposomes is a promising strategy to promote the induction of *Mtb* specific T-cells.

Marina Keil

I was born in 1988 in the beautiful town of Lindenfels. After school, I graduated from the University of Bayreuth with a BSc in Biochemistry. I continued my academic research and obtained my MSc in Biochemistry from the Ruhr University Bochum. Since July 2014, I have been working at the Institute of Biochemistry and Molecular Biology in Ulm.



Johannes Keller

I was born in Ulm in 1992. After leaving for an exchange year in New York, USA, and two more years in Regensburg, Bavaria, I moved back to Ulm to finish Medical School within the experimental medicine program of the Graduate School. Now I am working on my medical doctoral thesis at the Institute for Anatomy and Cellular Biology. I have always been fascinated with science and nature and am excited to be part of this program.

Characterization of the anti-apoptotic factors PPAN and PES1 in tumor cells with constitutive-active Wnt signaling and in NPM-mutated leukemia cells.

Wnt signaling regulates cell growth, proliferation and differentiation and thus plays a crucial role in development and disease. Consistently, it has already been demonstrated that several anti-apoptotic Wnt targets are upregulated in tumors with constitutively active Wnt signaling, for instance, in colon cancer and leukemia. The expression of Peter Pan (PPAN), Nucleophosmin (NPM) and Pescadillo (PES1) is directly induced by Wnt signaling and is required for proper 45S rRNA maturation in the nucleolus as well as cell growth. NPM is commonly mutated (35%) or misexpressed in AML patients and the mutated variant inhibits apoptosis. NPM is also known to be an interaction partner of the anti-apoptotic factors PES1 and PPAN. To understand the molecular mechanisms involved, I will investigate PPAN and PES1 in more detail concerning their potential role in tumors with constitutive-active Wnt signaling and NPM-mutated leukemia cells.

The development of novel nanoparticles as blood-brain barrier permeable drug carriers in the treatment of Alzheimer's disease

In our aging population, neurodegenerative diseases, such as Alzheimer's disease (AD), are on the rise. To treat these, we not only need the right medication but also a suitable transporter to cross the blood-brain barrier. Nanoparticles (NP) have been shown to do so if coated with specific glycoproteins. These nanoparticles will also be loaded with curcurmin, an enzyme able to cut amyloid-beta plaques. Accumulation of plaques and tangles are the two most prominent changes in Alzheimer's disease. This work will include the characterization of different NPs *in vitro* and *in vivo* to show their effects on plaque development in AD.

Kathrin Kennerknecht

Born in 1987, she started her PhD in April 2015 at the Institute of Medical Microbiology and Hygiene in the "MyTB-Lab" of PI Prof. Dr. Steffen Stenger. "MyTB-Lab" focuses on understanding host pathogen interactions in human tuberculosis. The key objective is to develop novel vaccination strategies against tuberculosis.

Samira Khalaji

Born in 1985, she completed her master degree in biomedicine. In July 2013, she started her PhD in the International Programme of Molecular Medicine at the institute of Experimental Physics under supervision of Prof. Kay-E. Gottschalk. The lab focuses on the impact of the environment on cellular properties, such as cell function and cell mechanics.

Design of liposomes for the delivery of vaccine antigens against tuberculosis

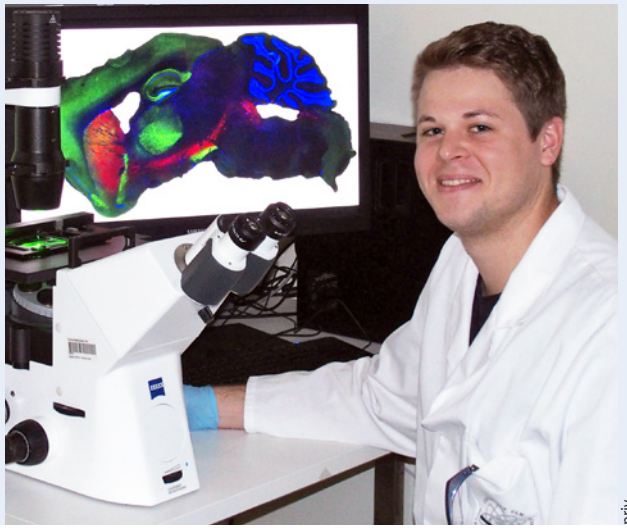
Tuberculosis remains the most deadly bacterial disease worldwide and the increasing frequency of multiresistant strains is aggravating the situation. Since the only available tuberculosis vaccine (BCG) is not sufficiently efficient to prevent the spread of tuberculosis, novel vaccine strategies are desperately needed. The majority of new vaccine approaches rely on protein antigens. Based on the fact that the cell wall of *Mycobacterium tuberculosis* contains an unusually high amount of lipids, the focus of this project will be on lipid antigens. A prerequisite for the activation of protective T cell responses is the efficient transport of antigens into macrophages. One promising approach is to deliver hydrophobic lipids via cationic liposomes. For example, lipoarabinomannan-containing liposomes ("LipLam") activate mycobacteria-specific T cells more efficiently than lipoarabinomannan alone. The aim of this project is to optimize the efficacy of lipid-based vaccines by strengthening innate and acquired immune responses. Firstly, the immunogenicity of the liposomes will be modified by incorporating Toll-like receptor agonists and macrophage-specific ligands. Secondly, T cell activation will be supported by including co-stimulatory molecules in the liposomal backbone. Ultimately, we expect to develop an efficient delivery and stimulation vehicle for unconventional lipid antigens, engendering efficient protection against tuberculosis infection *in vivo*.

Biophysical aspects of cell aging: do cells get stiffer with aging?

Biological aging is a multi-dimensional process that takes place over a whole range of scales, from the nanoscopic alterations within individual cells to transformations in tissues and organs, and even changes within the whole organism. On the single cell level, aging involves mutation of genes, differences in gene-expression levels as well as altered post translational modifications of proteins. A variety of proteins is affected and includes proteins of the cell cytoskeleton and migration machinery.

There are several techniques to study the cell cytoskeleton. However, one of the newest and most interesting methods is particle-tracking microrheology, which quantifies the mechanical properties of cells by monitoring the Brownian motion of individual particles imbedded in the cytoskeleton of the cells.

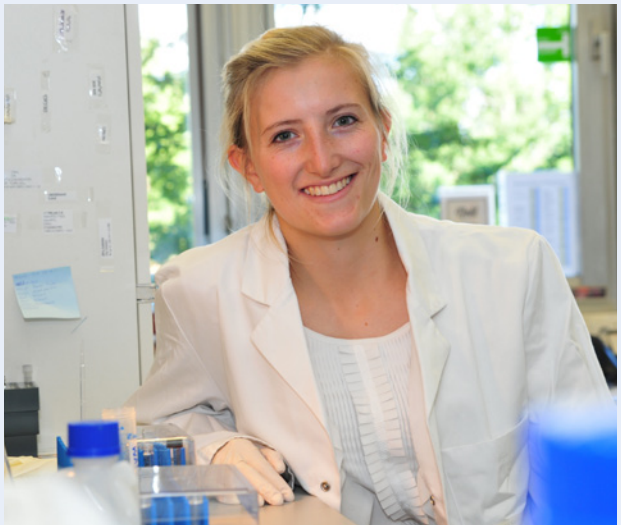
In my project, we are focusing on primary dermal fibroblasts isolated from young and advanced-age humans. Former studies reported on the stiffening of cells with age and employed other methods, e.g. AFM which characterizes the cortex tension of living cells, but our primary results do not agree with those studies. Therefore, we plan to apply other additional methods, such as AFM. Eventually, we will be able to interpret, compare and draw conclusions from our results.



priv.

Martin Kiechle

Born in 1987, I studied Biochemistry at Ulm University with a minor in Neurology at EPFL (École Polytechnique Fédérale de Lausanne) where I made the decision to stay in this research field. Now, I am researching Parkinson's disease in the lab of Junior Prof. Dr. Karin Danzer in the Department of Neurology.



Lena-Maria Kiem

Born in 1992 in Ehingen (Donau). For the next ten months, I will work on my dissertation at the Institute of Biochemistry and Molecular Biology under the direction of Prof. Dr. Michael Kühl, while Dr. Susanne Kühl supervises my work in the lab. My dissertation is being conducted within the framework of the study program in Experimental Medicine which is a doctoral program for medical students interested in engaging in research.

Characterization of a novel mouse model for the initiation and propagation of alpha-synuclein oligomerization in Parkinson's disease (PD)

PD is one of the most common neurodegenerative diseases worldwide with about 300,000 cases in Germany today. Histopathological studies showed abnormal intracellular protein aggregations in nerve cells, called Lewy bodies. These deposits are mainly composed of α-synuclein (α-syn). Accumulating evidence suggests that α-syn oligomers are secreted and taken up by neurons and that oligomers are the principle toxic species in PD and not Lewy bodies themselves. The concept of misfolded α-syn being transmitted in a prion-like manner has become more important in recent years and is supported by cell culture experiments and animal models. Up till now, the progression and propagation of α-syn oligomerization in the brain is not fully understood. In order to shed light on α-syn oligomerization *in vivo*, we generated two novel neuronal α-syn overexpression mouse models in a Tet-Off system-inducible manner, based upon a reporter protein-fragment complementation assay. In our mouse lines, α-syn is fused to the N-terminal half of either human Gaussia Luciferase or venusYFP and α-syn is fused to C-terminal half of human Gaussia luciferase or venusYFP. When α-syn starts to oligomerize, the reporter fragments will be in close proximity, complementary to an active enzyme or fluorescent protein.
In my PhD thesis, I will characterize the two novel mouse lines to gain a total perspective of our PD model system and its potential use in fundamental research.

Functional analysis of N4BP3 during neural development of Xenopus laevis

Ubiqutin Ligase Nedd4 is known to be required for axonal pathfinding of retinal ganglion cells in *Xenopus laevis*. In line, the Nedd4-binding-protein N4BP3 is also involved in neuronal branching during Xenopus embryonic development (Schmeisser et al., 2013). Another study showed that a missense version of N4BP3 is associated with intellectual dysfunctions in human children. In Xenopus, N4BP3 is expressed in the anterior neural tissue and the developing eye. In my work, I could show that loss-of-function in the anterior neural tissue of *Xenopus* leads to severe defects during eye and cranial cartilage development. Moreover, neural crest cell development is interfered in these embryos. N4BP3 depletion early in the embryo demonstrated inhibited marker gene expression in the eye and the brain as well. My future experiments will give more insights into the molecular mechanism of N4BP3 function during Xenopus neural development and whether there is a correlation between N4BP3 deficiency and the intellectual dysfunction shown in human.

Sebastian Karl Kieser

Born in 1991 in Stuttgart, I am working in the research laboratory of the Oncology group in the Department of Otorhinolaryngology, Head and Neck Surgery, Ulm University Medical Center under the supervision of Prof. Dr. Cornelia Brunner and participated in the doctoral study program in Experimental Medicine during the summer semester of 2015.

Nicole Kirsten (née Frank)

I was born in 1987 in Neu-Ulm, Germany. My interest in science, or more precisely, in cancer research was roused while completing my master's thesis during which I worked on aneuploidy and cancer. In 2013, I started my PhD at the Institute of Experimental Cancer Research under the supervision of Prof. Dr. Christian Buske. In addition to this, I am also working for the Ministry of Science, Research and Art for the state of Baden-Württemberg as a study ambassador.

Characterization of B cell development in the absence of Vav-proteins

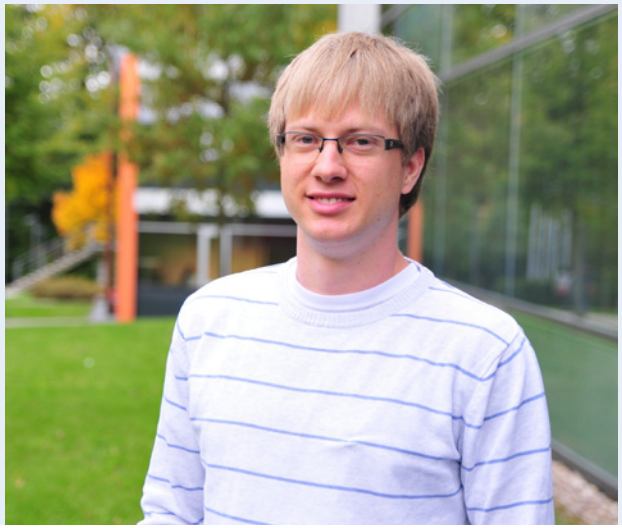
Vav-proteins are guanine nucleotide exchange factors for Rho-GTPases that are differentially expressed in cells of the hematopoietic system. In B cells, Vav1, Vav2 and Vav3 were identified. Although the role of Vav-proteins in B- and T-lymphocytes was addressed in several previous studies, so far the involvement of Vav-proteins in B cell development and function is still not completely understood.

The aim of the present thesis is the detailed investigation of Vav1 function in the development of B-lymphocytes, since we could show that a simultaneous deficiency in Vav1 and Btk (Bruton's Tyrosine Kinase) proteins leads to a dramatic enhancement of the effect of Btk alone, a well-known component of the B cell receptor-mediated signal transduction cascade. The absence of a functional Btk causes a severe B cell developmental defect in mice and humans that is characterized by a significant reduction in primary as well secondary immunoglobulin serum levels due to a marked reduction in peripheral B cell numbers. Since both Vav1 and Btk are components of the signalosome that builds upon B cell receptor engagement, the precise role of Vav1 in B cell receptor-mediated signal transduction at different stages of B cell maturation should be investigated. This work will increase our knowledge about the physiology of B cell development as well as the role of Vav-proteins in that process.

Influence of young and aged primary stroma cells on leukemic/ stromal interactions

The median age at diagnosis of acute myeloid leukemia (AML) is between 68 and 72 years. Aging seems to be a major risk factor for acute myeloid leukemia, but the mechanisms of the age-associated exponential increase in the incidence of leukemia are not known in detail. For this reason, we hypothesize that the aged niche promotes leukemia progression. The bone marrow microenvironment can be separated into two niches: the endosteal niche (inner surface of the bone cavity) and the vascular niche. Hematopoietic stem cells (HSCs) reside within these specialized areas. The regulation of HSCs are dependent on bone marrow stromal cells (BMSC) in the endosteal and vascular niches, which encompass a variety of cell types, such as osteoblasts, osteoclasts, endothelial cells, perivascular reticular cells, and mesenchymal stem cells. The maintenance and localization of HSCs are controlled by BMSC through the production of cytokines, chemokines and intracellular signals initiated by cellular adhesion. Like their normal HSC counterparts, leukemic stem cells in AML are presumed to reside in the niches in the bone marrow and this protects them against drug treatment. This chemotherapeutic treatment may be the cause of relapse following chemotherapy.

Based on this, this doctoral thesis intends to characterize the effect of stroma on leukemia progression and crisscross the impact of leukemic cells on its stromal microenvironment by utilizing the HOXA9-MEIS1 model in combination with young or aged primary BMSC.



Michael Kleemann

Born in Ulm in 1989, he studied Pharmaceutical Biotechnology at the Biberach University of Applied Sciences. His bachelor's thesis was focused on telomere length regulators. He went to Sigmaringen to study Biomedical Sciences and wrote his master's thesis about Integrin ‹5 in mesenchymal stem cells. In March 2015, he started his PhD at the Institute of Applied Biotechnology in Biberach.

Felix Klenner

I was born in 1984 in Offenburg, Germany. I studied biology in Freiburg and Ulm. I am a PhD student in the group of Prof. Dr. Gilbert Weidinger at the Institute of Biochemistry and Molecular Biology where I am currently working on my PhD thesis as a member of the International Graduate School in Molecular Medicine.

MiRNA targets in apoptotic pathways and their use as therapeutics

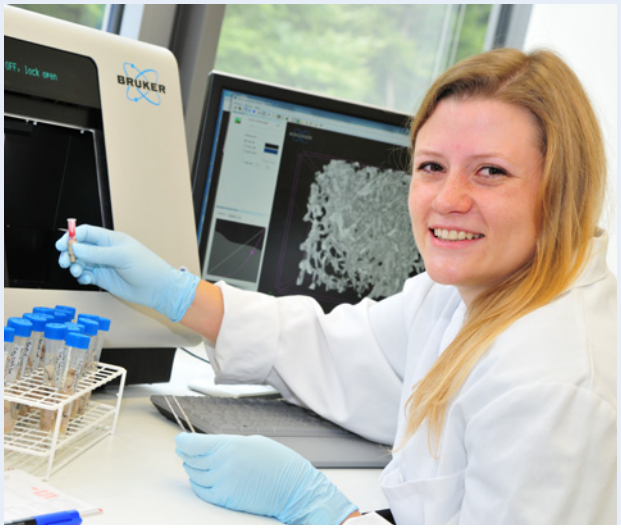
MicroRNAs (miRNA) are evolutionary conserved, small non-coding RNAs regulating mammalian gene expression by binding to their target mRNA. MiRNAs regulate biological processes that include cell proliferation and survival. Deregulation of miRNA expression can result in tumorigenic transformation or in a decrease of treatment sensitivity.
Apoptosis is a conserved, irreversible process that allows cells to undergo a highly controlled form of cell death. MiRNAs are involved in regulating the intrinsic and the extrinsic pathway of apoptosis. However, the final role of miRNAs in apoptotic signaling has yet to be fully understood. Modulating the expression of key molecular components of the cell-death machinery is an attractive strategy for cancer therapy. MiRNA mimics inherently target a number of different target mRNAs in a coordinated fashion. This provides a unique mechanism of action where the miRNA itself might become the therapeutic entity.
Based on the results of a functional high-content screening of miRNAs in CHO and human cancer cell lines, we want to identify targets of novel pro- and antiapoptotic miRNAs in cell-death pathways. In a translational approach, this knowledge might be used to create new anti-cancer therapeutics or diagnostics based on promising miRNA candidates.

The role of Wnt-signaling and Wnt-target genes in zebrafish caudal fin regeneration

The zebrafish *Danio rerio* shows an impressive regenerative potential compared to higher vertebrates by being able to completely restore lost or injured body parts, including heart and fins throughout its lifetime.
In particular, the caudal fin of *Danio rerio* has become a very successful model to study regeneration because of its accessibility to manipulation as well as its lifelong ability to quickly and robustly restore the original structure.
In our lab, we are interested in the Wnt-signaling pathway and especially in its role in caudal fin regeneration. Here, Wnt-signaling, though being essential for regeneration, seems to act indirectly by establishing secondary signaling centers that subsequently organize the process of regeneration.
In my PhD project, I focus on the transcription factor Prdm1a as a potential mediator for the effect of Wnt-signaling. Prdm1a is expressed throughout regeneration in distinct blastemal domains and could be shown to be transcriptionally regulated by Wnt-signaling during regeneration. Of special interest is an expression domain in a region associated with the formation of the bony elements of the fins. In this region, Prdm1a can transcriptionally affect genes involved in differentiation of osteoblasts, hinting towards a regulatory role in the bony portion of the regenerating fin. Further investigations are necessary to elucidate the effect of Prdm1a on the osteoblast lineage during zebrafish caudal fin regeneration.

Yvonne Koch

I was born in 1986 and work in the Department of Neurology in the working group of Prof. Otto. I am now in my fourth year of the PhD program.



Mascha Koenen

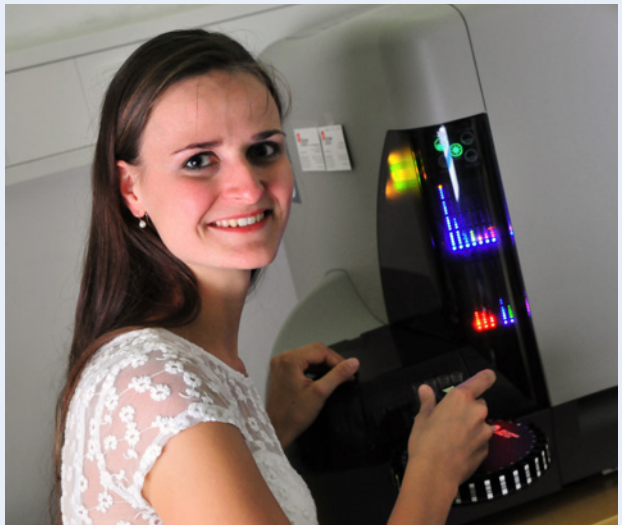
Born in 1988 in Heidelberg, Germany, I completed my bachelor's and master's studies in Biology at the Heinrich-Heine University, Düsseldorf. Since 2013, I have been a PhD student at the Institute of Comparative Molecular Endocrinology under the supervision of Prof. Dr. Jan Tuckermann at Ulm University, and am funded by the DFG SSP Immunobone. In spring 2014, I joined the International Graduate School in Molecular Medicine Ulm.

Influence of intracerebral superoxide dismutase 1 (SOD1) and α-synuclein aggregate injection onto SOD1 aggregation in a mouse model of amyotrophic lateral sclerosis (ALS)

The aim of the project is to characterize SOD1 aggregation in a mouse model of ALS after SOD1 or α-synuclein aggregates have been injected into the temporal cortex of young mice. As aggregation of SOD1 is believed to be one of the central disease-causing mechanisms in familial ALS, we thereby want to further elucidate the importance of this mechanism and its role in disease progression. Additionally, we want to find out if SOD1 aggregate-formation can be influenced by α-synuclein, a protein normally related to Parkinson's disease. This should help to solve the question whether a general mechanism exists by which amyloid structures refold proteins and favor their aggregation. To answer both questions, it is mainly the presence of SOD1 aggregates during different time points after injection that is analyzed in a motoric brain stem nucleus, an area distantly localized from the injection site and usually prone to SOD1 aggregation, by using immunohistochemistry and correlating it to the disease course of mice.

Molecular mechanisms of anti-inflammatory actions of the glucocorticoid receptor in arthritis.

Glucocorticoids (GC) with their potent anti-inflammatory properties are among the most frequently used drugs for the treatment of inflammatory diseases worldwide. Rheumatoid arthritis, a severe autoimmune inflammation of the joints, requires long-term GC therapy, which is associated with severe side-effects, e.g. osteoporosis, and compromises further therapy. GCs act via the Glucocorticoid Receptor (GR), a ligand-induced transcription factor that operates as monomer or homo-dimer and thereby targets various genes by different mechanisms. The current work of our group on a mouse model of arthritis revealed a crucial role of the GR homo-dimer in GC therapy, since GR dimerization-impaired mice (GR^{dim}) were refractory to GC therapy.
To identify possible GR dimer-dependent target proteins of GC therapy in arthritis, in cooperation with colleagues from the ETH Zürich, I performed an iTRAQ proteomics approach of inflamed ankles of GR^{dim} and GR^{wt} mice and will further validate the most promising differentially expressed proteins. To define the responsible cell type mediating these GR dimer-dependent anti-inflammatory effects of GCs, I will challenge various GR conditional knockout mice with GC therapy using the K/BxN mouse model of arthritis. In addition, I will analyze bone destruction and the bone density markers of these conditional KO mice by *in vitro* µCT and histological techniques in order to study the effects of GC therapy on bone during arthritis.



Ramona Kratzer

Born in 1988, she studied Molecular Medicine and graduated from Ulm University with a bachelor's and a master's degree while completing her master's thesis at the Autonomous University of Barcelona. She entered the International Graduate School in Molecular Medicine in the fall of 2012. Since then, she has been working on her PhD project in the Department of Gene Therapy in the research group of Florian Kreppel.

Jana Krieger

Born in 1988, I obtained my Master of Science in Biology, with its focus on Molecular Biology, from Ulm University in 2014. I became a member of Prof. Dr. Reinhold Schirmbeck's working group in the Department of Internal Medicine I at Ulm University Hospital while I was completing my bachelor's thesis. Since 2014, I have been in the PhD program of the International Graduate School in Molecular Medicine Ulm.

Improvement of adenovirus gene transfer vectors for genetic vaccination

In comparison to conventional vaccines, genetic vaccines can induce exceptionally strong CD8 T cell responses against pathogens. In particular, adenovirus (Ad)-based vaccine vectors demonstrated superior immune induction. Nevertheless, before routine clinical application, current vaccine vectors have to be improved with respect to multiple vector-host interactions.

To meet these needs, we apply technology developed in our lab to improve transgene expression and vector immunity. We combine two essential strategies. Transgene-based modifications relate to the pathogen to be protected from and will improve immune responses to pathogen-associated patterns (antigens). Virus capsid-based modifications refer to improved vaccine vector delivery and adjuvant functions. For example, membrane-active peptides, polymers or carbohydrates are attached to the viral capsid.

Subsequent analysis of innate and adaptive as well as vector- and antigen-directed immune responses will serve to understand how these modifications and interactions can enable a rational design of efficacious Ad-based vaccines.

Investigation of regulatory interactions between hepatocytes and antiviral CD8$^+$ T cells in 1.4HBV-S^{mut} tg mice

Hepatitis B virus (HBV) infections display a global major health problem. Five to ten per cent of adult patients and about 90% of infected newborns develop chronic infections that subsequently lead to a wide range of liver diseases and progress to liver cirrhosis and hepatocellular carcinoma (HCC). Patients who overcome HBV infections mount vigorous multispecific CD8$^+$ T cell responses to HBV, whereas low levels of CD8$^+$ T cells were detectable in chronically infected patients. Reconstitution of a CD8$^+$ T cell-mediated immunity by therapeutic vaccination is thus an attractive option for the specific control of chronic HBV infection. To characterize HBV-specific CD8$^+$ T cell responses in the presence of a liver that produces all HBV antigens, the 1.4HBV-S^{mut} transgenic (tg) line that harbors a replicating HBV genome in the liver was established. DNA vaccines efficiently induce HBV-C-specific (but not HBV-S-specific) CD8$^+$ T cell responses that transiently suppress HBV replication in the liver of 1.4HBV-S^{mut} tg mice. The project aims to elucidate systemic and intrahepatic regulatory effects that set off "exhaustion" of specific CD8$^+$ T cells in vaccinated 1.4HBV-S^{mut} tg mice. We will use 1.4HBV-S^{mut} tg mice crossed to well-defined tg or KO lines (deficient for co-inhibitory molecules, regulator cells or cytokines) and analyze the induction and function of antiviral CD8$^+$ T cells after vaccination with HBV-C-encoding vaccines or adoptive transfer of naïve HBV-C-specific BC10.3 CD8$^+$ T cells.

Ioanna Krikki

I was born in 1988 in Volos, Greece, and am currently a PhD student at the Department of Dermatology and Allergic Diseases as well as a member of the International Graduate School in Molecular Medicine Ulm. I received my bachelor's degree in Biology from the National and Kapodistrian University of Athens and my Master of Science in Biology from the Ludwig Maximilian University of Munich.

Astrid Kritzinger

Born in 1984, I studied Molecular Medicine at Ulm University. After completing my bachelor's degree, I continued with the consecutive master's program which I finished in summer 2013. Since 2014, I have taken a position as a PhD student at the Department of Gene Therapy in Ulm under the supervision of Prof. Dr. Stefan Kochanek. My project is in cooperation with the CNS Research of Boehringer Ingelheim Pharma GmbH & Co KG.

Role of histone H2A deubiquitinase Mysm1 in immune cell development and T helper cell differentiation.

Mysm1 is a histone-modifying enzyme that catalyzes the deubiquitination of K119 on histone H2A. Recent studies using Mysm1$^{-/-}$ mice revealed critical roles of Mysm1 in lymphopoiesis and early T cell development, suggesting possible involvement of Mysm1 in transcriptional activation of genes relevant to lymphoid development. Based on preliminary data indicating increased Foxp3 expression and changes in T cell populations in Mysm1$^{-/-}$ thymi and peripheral lymphoid organs, we hypothesize that Mysm1 may play a role in Th cell subset differentiation. My PhD project thus aims at analyzing T cell development in Mysm1-deficient mouse models and Mysm1 transcriptional mechanisms by *in vitro* and *in vivo* approaches. The data will be correlated with human inflammatory and immunodeficiency conditions. *In vitro* Th differentiation assays will be performed to assess the role of Mysm1 in Th cell subset specification. To dissect whether defective lymphoid development is due to an intrinsic requirement of Mysm1 in lymphocytes or to defects in HSCs, a newly generated mouse strain (CD127-Cre:Mysm1^{tm1a}) with lymphoid-specific deletion of Mysm1 will be analyzed for alterations in lymphoid development and differentiation. This project will improve our understanding of the role of histone modifications in lineage specification of T cell subsets and aid the development of therapies for autoimmunity, infections and cancer.

Development of a leucine-rich repeat kinase 2 in vivo Parkinson's disease model by intrastriatal injection of high-capacity adenoviral vectors

Mutations in the leucine-rich repeat kinase 2 (LRRK2) gene are the most common genetic cause of Parkinson's disease (PD). The most prevalent mutation, G2019S, leads to an increased kinase activity and there is great hope that pharmaceutical inhibition of LRRK2 could help patients with PD. Transgenic LRRK2^{G2019S} rodent models generally have a very mild phenotype with disturbances in the homeostasis of the nigrostriatal dopaminergic system that emerge only in aged mice. Two approaches with viral LRRK2^{G2019S}-harboring vectors showed that intrastriatal injection can induce degeneration of dopaminergic neurons in the substantia nigra (the hallmark of PD) more efficiently than is seen in transgenic animals.

We will now use high-capacity adenoviral vectors for intrastriatal injection because they are ideally suited for long-term expression of a transgene. Furthermore, we want to express LRRK2$^{G2019S\ or\ D1994A\ =\ kinase\text{-}dead}$ not only in neurons, as has been done by others, but ubiquitously in the striatum. This might reflect the natural situation better since endogenous LRRK2 is expressed in neurons, astrocytes and microglia. LRRK2 mutations cause late onset PD, implicating that the aged brain can no longer cope with LRRK2-induced cellular malfunctions. Therefore, we further plan to compare the effects of intrastriatal vector injection in young and aged mice over time.

Carsten Markus Kröger

Born in 1987, he started his scientific career with a BSc in Molecular Biomedicine in Bonn and continued with his MSc in Molecular Medicine in Erlangen. Currently, he is enrolled in the International Graduate School in Molecular Medicine Ulm and working on epigenetics and hematopoietic stem cells in the Department of Dermatology and Allergic Diseases of Ulm University.

Jochen Kroner

Born in 1987, he studied Biotechnology and Biomedical Science and started his PhD program at IGradU in April 2014. He is currently working at the Institute of Orthopedic Research and Biomechanics where he is focusing on the influence of the immune system on bone metabolism and fracture healing.

Mysm1 and the p53 axis

Beginning with the discovery of DNA methylation and, subsequently, with histone modifications such as acetylation and methylation, the field of epigenetics is now a rapidly growing area of active research. Recently, the role of histone ubiquitylation has emerged in epigenetics and is implicated in several biological processes. Histone H2A ubiquitylation has been shown to be a major event in the response to DNA damage and has been implicated in the regulation of gene transcription. The reversal of ubiquitination marks is of equal importance in these processes. In the past, our group and others defined the role of the histone H2A-specific deubiquitinase Mysm1. Work with mouse knockout mutants revealed an implication of Mysm1 in early T cell development, B cell development, NK cell maturation, and hematopoietic stem cell maintenance. Mutations occurring in humans closely resemble the murine phenotype. The murine knockout phenotype was largely abolished by concomitant knockout of the tumor suppressor p53. This PhD project will focus on further elucidating this interaction of Mysm1 and the p53 pathway and, additionally, will investigate the complex interplay of histone H2A ubiquitylation and other histone modifications.
This PhD project will employ a combination of mouse models, ChIP experiments and immunofluorescence imaging techniques to elucidate the role of Mysm1 in the maintenance of the hematopoietic stem cell pool under normal and malignant conditions in murine and human model systems.

Analysis of early immune responses and the role of mast cells in fracture healing

Mast cells belong to the immune system and are located in proximity to blood vessels and nerves in tissues at the interface between the body and the external environment. Their biological functions range from direct defence mechanisms to immunomodulation. The potent role as effector and modulatory cells is based on their ability to synthesize various substances that differ in potency and biological activity. Preformed granule-associated mediators as well as *de novo* synthesized cytokines can be released upon stimulation.
Aside from their role in immunological responses, they are also associated with angiogenesis and tissue remodeling. However, mast cells also seem to influence bone metabolism since patients with systemic mastocytosis exhibit a decreased bone mass. Additionally, some phenomenological publications have shown the presence of mast cells during fracture healing.
Therefore, this project aims to characterize the early inflammatory phase of fracture healing and, specifically, the impact of mast cells on bone regeneration. Fracture healing is investigated in a newly generated mouse model of constitutive mast cell deficiency by using a standardized osteotomy of the femur which is stabilized by an external fixator. Extensive analysis during the time course of fracture healing will answer questions whether mast cells modulate the early immune responses and, specifically, influence bone formation in the fracture callus.

Kathrin Krowiorz

I was born in Munich in 1983 and studied Biology at the Technical University of Munich (TUM) with my focus on Biochemistry and Cell Biology. As a student of the International PhD Programme in Molecular Medicine, I am working at the Department of Internal Medicine III in the group of Florian Kuchenbauer.

Alexandra Dorothea Krüger-Haag

Born in 1988, I studied Biology at Ulm University and completed the bachelor's and consecutive master's program in January 2015. Due to the fact that I was conducting my master's thesis at Rentschler Biotechnologie GmbH, I took a special interest in biotechnological research. In February 2015, I started my PhD studies at the Department of Gene Therapy by focusing on production systems of AAV vectors.

Modulation of normal and malignant hematopoiesis through microRNAs (miRNAs)

MiRNAs are essential for maintenance and differentiation of normal hematopoietic cells, and their dysregulation is strongly implicated in leukemias. The aim of the project is to identify novel tumor suppressor and oncogenic miRNAs in the context of acute myeloid leukemias (AMLs). We reason that tumor suppressor miRNAs are upregulated in lineage-committed cells, when compared to hematopoietic stem and progenitor cells (HSPCs), and downregulated in AML. We expect oncogenic miRNAs to be upregulated in AML and highly enriched in HSPCs. Based on two complementary miRNA expression screenings in normal hematopoiesis and AML, we select potent candidate miRNAs. Using the 32D cell model of granulocyte-colony stimulating factor (G-CSF) -induced differentiation, we analyze the influence of the candidates on myeloid differentiation. To identify candidates that are able to modulate stem cell function *in vivo*, lentivirally transduced HSCs are transplanted into lethally irradiated recipient mice. In the Hoxa9Meis1a AML model, the effect of the miRNA candidates on proliferation, apoptosis and cell cycle is analyzed *in vitro*. In bone marrow transplantation assays, we assess their *in vivo* ability to act either as tumor suppressors and delay Hoxa9Meis1a-mediated leukemogenesis or to act as oncogenes and accelerate leukemogenesis. By the identification of targets, we want to reveal signaling pathways and mechanisms underlying the oncogenic and tumor-suppressive functions, respectively.

Development of an improved production system for AAV vectors.

Adenovirus-associated virus (AAV) shows qualified properties to serve as a transfer vector in gene therapy. One promising strategy for vector production is the usage of stable producer cell lines, since they provide the advantage of high titers and scalability. Yet, AAV depends on a co-infection with a helper virus, such as adenovirus, to propagate and establish a productive life cycle. However, an infection with a replication-competent helper virus harbors the disadvantage of contaminated rAAV stocks, requiring elaborate purification and validation steps. Using life-cycle-defective adenovirus mutants to provide the helper functions would allow for an entirely infection-based production system for rAAV, reducing subsequent downstream processes and therefore increasing suitability for large-scale biopharmaceutical production by enhancing safety and efficiency. Consequently, a stable producer cell line for rAAV manufacturing needs to be established in order to characterize different types of genetically modified adenovirus mutants in respect of their applicability for efficient rAAV packaging.

priv.

Marc Krüger

Born in 1987, I am currently participating in the joint PhD program at Ulm University and the University of Padua, and offered by the International Graduate School in Molecular Medicine. My PhD thesis is conducted in the working group of Prof. Knippschild at the Institute of General and Visceral Surgery at Ulm University Hospital.

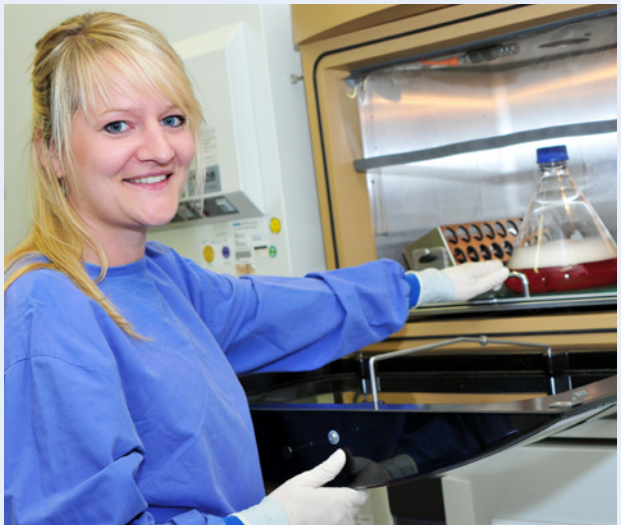
The role of CK1 in neurodegenerative diseases and the development of new pharmaceutical approaches to inhibit CK1 activity

Among the first protein kinases in eukaryotes that have been described are Casein Kinases 1 (CK1), a family of ser/thr-specific protein kinases. CK1 is ubiquitously expressed and found in many eukaryotes ranging from yeast to humans. Since they are involved in the regulation of various cellular processes, their activity has to be tightly regulated by various mechanisms, including interaction with cellular proteins and cellular structures on a protein level. It has generally been accepted that deregulation of CK1 resulting in overexpression plays an important role in the development of neurodegenerative diseases, especially in tauopathies such as Alzheimer's disease (AD). Whereas CK1δ plays a critical role in fibrillar lesions through phosphorylation of tau, CK1ε interacts with phosphorylates APP and thereby increases the Aβ production.

During the course of my PhD thesis I will address two pharmaceutical approaches to inhibit CK1 activity.

Firstly, I will focus on small molecule inhibitors that provide an ever-growing platform for the treatment of diseases related to deregulation of kinases.

Secondly, I plan to identify peptides that are able to inhibit protein-protein interactions.



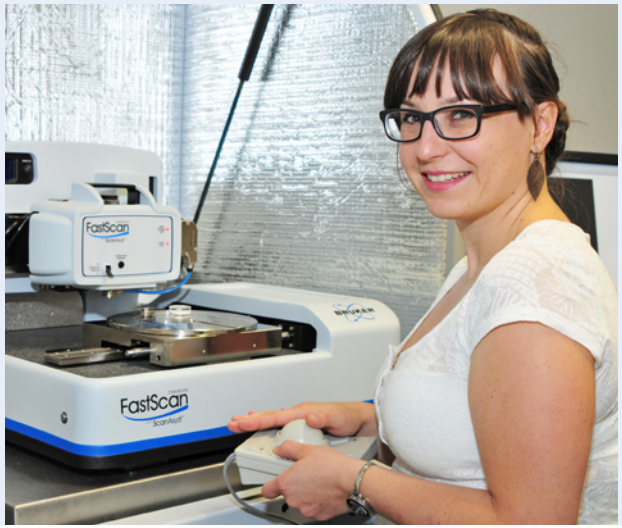
Lea Krutzke

Born in 1985, I finished my bachelor's program in Biology in 2010 in Karlsruhe. To focus my studies on medical research, I applied for the International Master's Programme in Molecular Medicine at Ulm University and graduated in 2012. Subsequently, I started my PhD studies in the framework of the International Graduate School in Molecular Medicine in the Department of Gene Therapy.

Unraveling the molecular basis of adenovirus interactions with non-cellular and cellular host blood components

Adenovirus type 5 (Ad5) is a very potent gene transfer vector for gene therapeutic approaches. However, its clinical applicability is limited by multiple non-target vector-host interactions and, in particular, with cellular and non-cellular host blood components. These interactions can result in significant vector loss and adverse effects. However, systemic delivery of vector particles is mandatory for various applications targeting large organ systems, e.g. skeletal muscle or disseminated tumors and metastasis.

The overall aim of my PhD thesis is to identify capsid areas of Ad5 involved in vector-blood interactions, to understand the underlying mechanisms and to manipulate them. Therefore, I generated a set of mutant vectors carrying different genetic and chemical capsid modifications and subjected them to various *in vitro* and *in vivo* assays that are designed to map specific interactions to defined capsid positions. Finally, based on the knowledge gained, strategies to avoid unwanted or to exploit favorable vector-blood interactions will be evaluated to improve vector stability in blood.



Katarzyna Maria Krzemien

Born in 1986 in Poland, she is working on her PhD thesis in the group of Professor Jens Michaelis at the Institute of Biophysics. Currently, she is in her final year of the International PhD Programme in Molecular Medicine at Ulm University. The scope of her studies is the use of advanced super-resolution and single molecule techniques to resolve the chromatin structure.

Céline Pfeifer

Galina Kulstein

I was born in 1987 and finished my diploma in Biology in 2012 at the Johannes Gutenberg University in Mainz. My major research is focused on forensics, anthropology and genetics. In my work, I have the possibility of combining all of these and I am doing my PhD at the Institute of Legal Medicine in the Department of Forensic Genetics. I started the IGradU program in the autumn of 2013.

The structure of nucleosomal arrays towards super-resolution fluorescence studies

Chromatin is the DNA storage mechanism that has to fulfil two functions: a high compaction of DNA and fast access to the genomic information. DNA storage in eukaryotic cells exhibits several levels of compaction that has one important structural feature known as the chromatin fiber. *In vitro*, different structures of chromatin arrays have been proposed but none of them is unambiguous.

In spite of large experimental efforts in recent years, many questions about the packing of DNA are waiting for an answer. Solving these problems will be indispensable for the understanding of basic cellular processes involving the DNA.

The cross section of a single nucleosome is about 10 nm; a condensed chromatin fiber *in vitro* has a cross section of about 30 nm and the length of an array is in the order of 100 nm. Structures of such small dimensions cannot be visualized with a traditional light microscope due to the diffraction limit. In recent years, a number of super-resolution fluorescence techniques have been invented to resolve details of structures smaller than 200 nm.

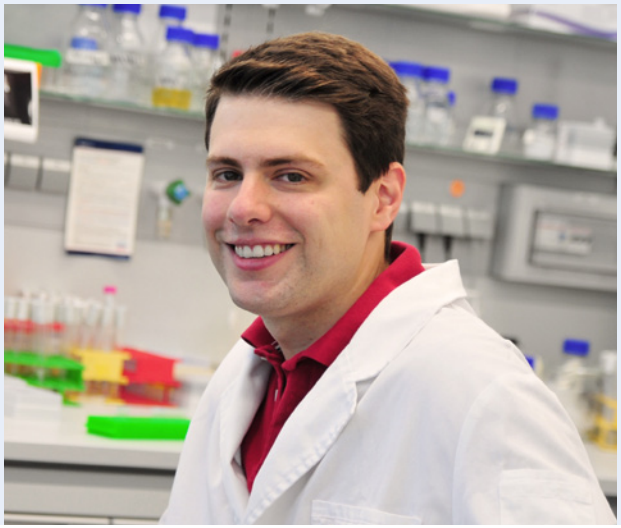
The aim of my thesis is to use a unique combination of single molecule FRET with super-resolution microscopy to unravel the structure of chromatin fibers. By means of protein engineering and the application of novel protein-labeling strategies, I prepared fluorescently labeled chromatin fibers suitable for fluorescent imaging and also use atomic force microscopy (AFM) as a tool for the control of chromatin arrays produced *in vitro*.

MicroRNA profiling for body fluid and tissue identification of forensic samples

The task of forensic genetics includes the assignment of a perpetrator to a crime scene related stain. Additionally, the identification of the cellular origin of the biological stain can provide further insight into crime scene related events. Common forensic relevant biological fluids and tissues are blood, saliva, semen, vaginal epithelial cells, menstrual blood, and skin. Current methods for their identification comprise mainly immunological approaches based on antibody antigen reactions or chemical tests. Unfortunately, some of those tests have disadvantages, e.g. lack of sensitivity and specificity or sample consumption. Recent advances have led to the exploration of new markers, especially microRNAs (miRNAs) which are small (18-24 nucleotides) non-coding molecules that seem to be promising candidates for body fluid and tissue identification. They show a tissue-specific abundance and are more resistant to degradation because of their small size. My thesis aims to establish a miRNA-based approach for body fluid and tissue identification. The application should accomplish the reliable analysis of mixed as well as environmentally challenged stains. This can be achieved by implementation of a miRNA-qRT-PCR process into the current DNA-oriented forensic workflow. This would allow a simultaneous determination of type/origin of biological material via RNA and the assignment of the trace to a perpetrator using DNA.

Monika Kustermann

Born in 1989, I am a second year PhD student in the International PhD Programme in Molecular Medicine. I am working in the Department of Internal Medicine II (Molecular Cardiology). Our lab is mainly focusing on the genetic and molecular networks of heart development and function. The long-term goal of our research is the development of new therapies for heart/muscle diseases.



Jochen Kustermann

Born in August 1988, I am a second year PhD student of the International Graduate School in Molecular Medicine. I work in the Institute of Molecular Genetics and Cell Biology. In our lab, we mainly focus on cell polarity establishment and maintenance. Furthermore, we try to understand how cell polarity is linked to other cellular processes.

Dissecting the pathogenesis of myofibrillar myopathies

Myofibrillar myopathies (MFMs) are inherited, progressive diseases of the heart and skeletal muscle that often lead to physical disability and premature death. The patients manifest pathologic desmin-positive protein aggregates, degenerated myofibrils, and mitochondrial abnormalities. Several MFM-causing gene mutations are known, but the molecular pathomechanisms that translate them into the myopathic phenotype are nevertheless still poorly understood. The aim of my PhD project is to establish zebrafish models to dissect the pathomechanisms of known and novel MFM disease genes. One of these MFM disease-causing genes is the *valosin containing protein (vcp)*. VCP is a member of the AAA-ATPase superfamily of chaperone-like proteins and is important for the protein degradation system. The functional and morphological analyses of VCP zebrafish morphants display a progressive skeletal muscle myopathy with less myofibers and severe degenerative musculature. Loss of VCP leads to an enrichment of rimmed vacuoles as well as filamentous inclusions, which might represent immature autophagosomes and an accumulation of polyubiquitinated proteins in the skeletal muscle. VCP is one of the best studied type II AAA ATPases but, up till now, no therapeutic treatment is available. Therefore, I am generating TALEN VCP knockout and also transgenic zebrafish lines which overexpress human IBMPFD/MFM myopathy mutations.

Novel players in secretory pathway polarization

The establishment of cell polarity is a critical event in all living cells and forms the basis for many biological processes such as cell migration, asymmetric cell division, and cellular aging and communication. For decades, the ascomycete *Saccharomyces cerevisiae (S. c.)*, or budding yeast, has been used as a powerful model organism to study the basic mechanisms of cell polarity establishment and maintenance. The master regulator of cell polarity establishment in S. c. is the small GTPase Cdc42. In its active state, Cdc42 localizes to the plasma membrane and defines the site of polarized growth. There, Cdc42 reorganizes the cytoskeleton and thereby regulates intracellular transport processes. In my thesis, I basically focus on secretory pathway polarization on the level of protein-protein interaction networks. I want to understand how post-golgi vesicles can be directed to clusters of active Cdc42 at the membrane.
So far, I have been able to identify proteins that directly interact with both Cdc42 and proteins which are essential for vesicle tethering and fusion. Furthermore, I could show that those proteins are essential for vesicle fusion at the membrane. I hope that my work will lead to a more detailed understanding of the connection between cell polarity establishment and exocytosis, and all resulting physiological processes and related diseases.

Simon Markus Langer

Born in 1987, Simon studied Biology and Molecular Medicine at Ulm University and earned his MS degree in 2012. He started his PhD in November 2013 at the Institute of Molecular Virology under the supervision of Frank Kirchhoff and Daniel Sauter. He joined the International Graduate School in Molecular Medicine in the spring of 2014. Simon eagerly hopes to become a Nobel laureate one day.

Dominik Langgartner

Born in 1987 in Burghausen, I completed my bachelor's and master's studies in Biology and Neuroscience at the University of Regensburg.
I am a second year PhD student of the International Graduate School in Molecular Medicine and working in the laboratory of Molecular Psychosomatics at the Clinic of Psychosomatic Medicine and Psychotherapy, Ulm University Hospital, under the supervision of Prof. Dr. Stefan Reber.

Characterization of HIV-1 Rev1-Vpu fusion proteins

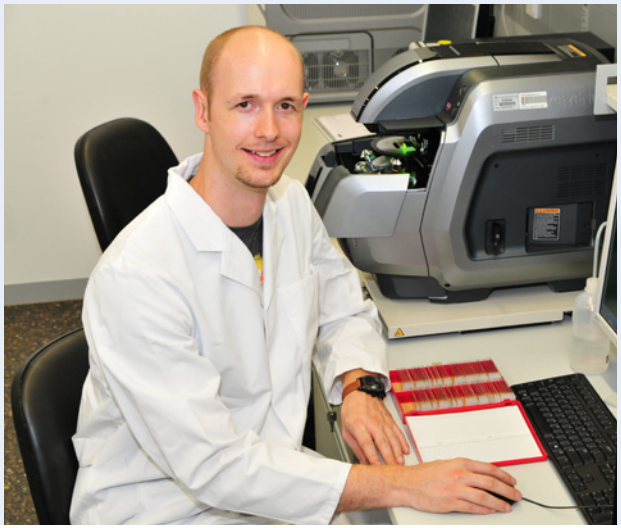
The genome of HIV-1 comprises structural (*gag, pol, env*), regulatory (*rev, tat*) and accessory genes (*vif, vpr, vpu, nef*). The expressed proteins build the viral particle, enable efficient replication *in vivo* and equip the virus with tools to evade or counteract the antiviral immune response. In 2010, Kraus et al. described an unusual gene arrangement in which the first exon of *rev* (*rev1*) and the vpu gene are in the same reading frame without an intervening stop codon. This polymorphism is present in about 10% of all HIV-1 strains worldwide.
Whereas the functional activity of the Rev1-Vpu fusion proteins remain to be investigated, the function of both parental proteins has been characterized in detail: the regulatory protein Rev facilitates the export of unspliced or singly spliced viral RNA from the nucleus into the cytoplasm so that the structural proteins and the RNA genome can be produced. The accessory protein Vpu, among others, counteracts the restriction factor tetherin to enable efficient release of progeny viruses from infected cells and down-modulates the viral receptor CD4 to prevent superinfection. So far, expression of a Rev1-Vpu fusion protein has not been demonstrated in HIV-1-infected cells and it remains unclear whether such fusion proteins have the ability to perform any of the functions ascribed to Vpu or Rev. Consequently, the high prevalence of the *rev1-vpu* polymorphism and the important functions of Vpu and Rev in the viral replication cycle make it an important and interesting subject of study. Langer et al 2015

Effects of chronic psychosocial stress in C57BL/6 mice: a closer look at the hypothalamic-pituitary-adrenal (HPA) axis and the influence of housing conditions

Chronic stress poses a constantly increasing burden in our modern society. A growing body of evidence underpins that chronic psychosocial stress is an acknowledged risk factor for the development of various affective and somatic disorders. However, to date, the underlying physiological and molecular mechanisms are far from being understood. An approach to give more insight into this issue is the use of appropriate animal models that adequately mimic the human situation.
In my study, I use the so-called "chronic subordinate colony housing" (CSC) model, a preclinically validated model for chronic psychosocial stress in male mice. Besides the development of somatic and affective disorders, CSC leads to a reduced glucocorticoid (GC) signaling. The underlying processes at the level of the HPA axis have not been entirely investigated so far. One main aim of my project, therefore, deals with investigating the mechanisms behind CSC-induced alterations at the level of the HPA axis, with the main focus on the adrenal glands.
Furthermore, it is known that differences in animal housing conditions can have tremendous effects on the experimental outcome. To ensure reproducibility in research, it is important to elucidate possible influential environmental parameters. Therefore, the second aim of my project deals with revealing the influence of different factors in animal housing on the development of CSC-induced alterations.

Hanna Leins

I was born on 17 December 1987 in Filderstadt. After completing my studies in Biochemistry at the Eberhard Karls University, Tübingen, I started my PhD in 2013. I am working in a cooperation project run by AG Schirmbeck (Internal Medicine I) and AG Geiger (Institute of Molecular Medicine and Stem Cell Aging). I am also enrolled in the International Graduate School in Molecular Medicine.



Pascal Lösing

Born in 1986 in the small town of Vreden in North Rhine-Westphalia, Pascal worked as a data manager and programmer after his A levels before studying Applied Biology. After completing his bachelor's degree in Scotland, he finished his master's in Molecular Medicine here in Ulm. He is now a third year PhD student under the supervision of Professor Bernd Knöll and works at the Institute of Physiological Chemistry.

Enhancing and restoring immune function in the aged hematopoietic and immune system

With age, immune function declines. This is referred to as immunosenescence and results in an increased susceptibility to infections, increased onset of autoimmune diseases and cancer in the elderly.

One of the most efficient and cost-effective ways to protect people from morbidity and mortality due to infections is vaccination. But current vaccines and vaccination strategies are less effective or completely ineffective due to immunosenescence.

To restore adequate immune responses in older adults, new approaches are indispensable. It is well known that the aging of long-term hematopoietic stem cells (LT-HSCs) contributes substantially to immunoaging. Thus, I analyze the effect of a new rejuvenation approach of aged LT-HSCs on the immune function. Consequently, my efforts concentrate on the adaptive immune system. Furthermore, I am testing new vaccination strategies to enhance immune response to vaccines in the elderly.

Rejuvenation of the aged hematopoietic system in combination with special vaccines could lead to an increased understanding of immunosenescence and help to restore, at least partially, immune competence in the elderly.

The role of the serum response factor in a murine model of temporal lobe epilepsy

Temporal lobe epilepsy (TLE) is the most common form of epilepsy, in which most patients are resistant to common antiepileptic drugs. To investigate TLE, we use the pilocarpine mouse model to chemically induce seizures and to mimic many characteristic features of human TLE in a murine system.

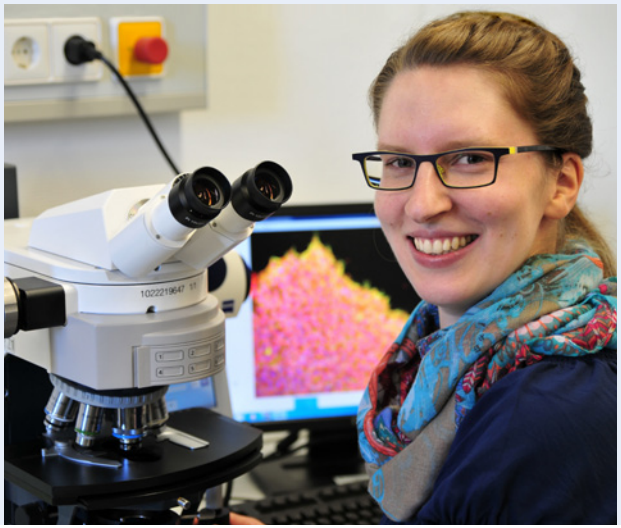
Our main interest is the influence of the transcription factor known as the serum response factor (SRF) on the development of acute seizures and on long-term changes in epileptic animals. SRF is known to control the expression of immediate early genes (IEGs) which are upregulated in response to seizures. Furthermore, SRF controls various aspects of neuron motility, including the guidance of mossy fibers.

To investigate the role of SRF in the pilocarpine model of TLE, we are using conditional SRF knockout mice and are closely investigating histological, transcriptional and behavioral changes.

This research could indicate a link between SRF and TLE, and holds the potential for discovering novel protective mechanisms against TLE.

Edina Lump

Born in 1987, she is conducting her research for her PhD thesis in the group of Jan Münch at the Institute of Molecular Virology, Ulm University Medical Center. Before this, she studied Biochemistry and Molecular Biology at the University of Bayreuth. She joined the PhD program of the Graduate School in October 2012.



Anne-Kathrin Lutz

I was born in January 1989 and joined the Graduate School in Molecular Medicine Ulm in April 2014 after receiving my master's degree in Molecular Neurosciences at Heidelberg University. Currently, I am in the second year of completing my PhD thesis at the Institute for Anatomy and Cell Biology under the supervision of Prof. Dr. Tobias Boeckers and Dr. Maria Demestre.

A molecular tweezer antagonizes seminal amyloid and HIV infection

Human semen, the main vector for sexual HIV transmission, contains amyloid fibrils that greatly enhance viral infection *in vitro*. These amyloids form by the self-assembly of peptides derived from the abundant semen proteins of prostatic acid phosphatase (PAP) and semenogelin 1/2 (SEM1/2). They are positively charged and facilitate virion attachment to the target cell and subsequent infection. Hence, they might be important for sexual HIV transmission. Their counteraction provides a novel strategy to reduce viral spread in humans.

In my thesis, I examine whether the molecular tweezer, CLR01, previously described as an inhibitor of assembly and toxicity of amyloids, is able to antagonize semen-mediated HIV infection enhancement. To investigate CLR01's effect on seminal amyloids, I take advantage of electron microscopy, amyloid-specific dyes and Zeta-potential measurements. I use confocal microscopy and infection assays to determine how CLR01 affects the capture of virions by fibrils and semen-mediated infection enhancement. So far, I have found that CLR01 inhibits the assembly of PAP and SEM peptides and remodels preformed fibrils. CLR01 neutralizes the fibrils' cationic surface charge, impedes formation of virus-amyloid complexes and diminishes semen-mediated enhancement of HIV infection. Notably, CLR01 also directly inhibits HIV and other enveloped viruses by disrupting their membranes without showing any cytotoxicity. With its dual anti-amyloid and antiviral activity, CLR01 has the potential for becoming a novel microbiocide candidate.

Characterization of SHANK2 and SHANK3 mutations in iPSC culture systems

The Shank family members, SHANK1, SHANK2 and SHANK3, are scaffolding proteins that form large protein complexes in the postsynaptic density of excitatory glutamatergic synapses. They are involved in multiple processes that include synapse formation, remodeling and plasticity. Mutations in all three members of the Shanks have been linked to Autism Spectrum Disorders (ASD), a group of developmental disorders that is characterized by deficits in social interaction and repetitive behavior.

This PhD thesis focuses on human SHANK2 and SHANK3 mutations by using induced pluripotent stem cells (iPSCs). iPSCs can easily be generated from proband keratinocytes and offer a wide range of application as they can be differentiated into any cell type of interest. In this project, iPSC-derived motoneurons and muscle cells are generated and characterized.

One of the first presenting symptoms of children suffering from deletions in SHANK3 is hypotonia. iPSC-derived muscle cells and motoneurons are used to mimic the formation of the neuromuscular junction to elucidate the role of SHANK3 not only in central but also in peripheral synapses. An isogenic SHANK3 patient iPS cell line, generated using CRISPR technology, enables direct patient-control comparison. Mutations in SHANK2 are less common than in SHANK3 but interestingly, SHANK2 and SHANK3 deletion patients show similar symptoms. Therefore, the comparison of SHANK3 and SHANK2 mutations, and the analysis of similarities will deepen our knowledge about the Shanks, especially in ASD.

Katharina Mack

I have been a member of the International Graduate School in Molecular Medicine since November 2012 and am working in the lab of Prof. Frank Kirchhoff at the Institute of Molecular Virology.

HIV-1 group O has evolved Nef as an antagonist of the antiviral factor tetherin

In my PhD project, I am working with the antiviral factor tetherin. This transmembrane protein keeps budding virions attached to the cell surface by inserting one of its two membrane anchors into the membrane of the virus, while the other membrane anchor stays in the host cell membrane. The precursor viruses of HIV, which infect apes and monkeys, use their accessory protein Nef to counteract simian tetherin. It is commonly believed that the human orthologue of tetherin is resistant to the HIV accessory protein Nef because of a 5 amino acid deletion in its cytoplasmic tail. The pandemic group M has therefore switched to the accessory protein Vpu to antagonize tetherin. I was able to show that HIV does not necessarily have to switch to another protein to counteract tetherin. Nef proteins of HIV-1 group O target a region adjacent to the 5 aa deletion and are thus able to downmodulate tetherin from the cell surface. This decreases interferon sensitivity of HIV-1 by enhancing virion release from primary human CD4+ T cells.
That the HI-virus does not necessarily have to switch from Nef to another protein shows the enormous plasticity of the virus and makes further transmissions from apes to humans more likely than was previously anticipated.

Sarah Mackert

I was born on 26 December 1991 in Heilbronn. In October 2014, I started to work on my doctoral thesis at the Institute for Anatomy and Cell Biology under the supervision of Prof. Tobias Böckers and Michael Schön. Since February 2015, I have been a participant in the study program in Experimental Medicine at the International Graduate School in Molecular Medicine Ulm.

Optimization and advantages of (electrophoretic) tissue clearing via the new method, CLARITY

Biological specimens are three dimensional, but, because of the obscuring effects due to light scattering, whole-organ imaging is problematic. With a varying degree of success, efforts to eliminate the scatter by “clearing” the tissue have been ongoing for over a century. In my doctoral thesis, I focus on one of the latest and most promising innovations in this field, namely, the electrophoretic tissue clearing via CLARITY.
CLARITY was introduced in 2013 and developed in the Deisseroth lab at Stanford University. The method is used to transform an intact tissue into an optically transparent and permeable form by replacing the lipid bilayer of plasma membranes with a nanoporous hydrogel.
During this procedure, all relevant biomolecules and structures are described to remain unchanged and accessible to antibody labeling and other histological treatments. Moreover, high resolution three-dimensional imaging without damage to the sample is now possible. This is tremendously important for a better understanding of the complexity of neuronal networks.
Hence, CLARITY provides both complete structural analysis and molecular phenotyping to gain full insights into the relationships and functional mechanisms of biological systems. In short, this might lead to new possibilities in medical research, especially in the area of neurodevelopmental and neurodegenerative disease.
In addition, I am elaborating on the advantages and disadvantages of immunoelectron microscopy on CLARITY-treated tissue.

Lars Maerz

Lars began his studies at the University of Konstanz and the University of Freiburg. His graduation at Boehringer led him to Ulm where he started his PhD at the Institute of Biochemistry and Molecular Biology. He performs competitive sports, such as soccer, to maintain his relationship with friends and family and remains an active member in his hometown's soccer club both as a player and a trainer of a women's team.

priv.

Nicolai David Marroquin Nisch

Born in 1988, he studied Molecular Medicine at Ulm University and, in 2012, he entered the Fast Track PhD program. He is working on an interdisciplinary cooperation project between the Institute of Human Genetics and the Department of Neurology. His PhD project aims at unraveling the genetic architecture of amyotrophic lateral sclerosis (ALS).

Identification of new signal pathways implicated in heterotaxy-driven congenital heart diseases.

A failure to establish the left-right axis during early embryonic development is commonly associated with the development of heterotaxy syndrome (HS). Typical manifestations of HS include cardiac anomalies, splenic abnormalities and other defects such as irregular gut looping. Of all these congenital malformations, congenital heart defects compromise the most serious complication and often require surgery within the first week of life.

To identify new molecules and signal pathways implicated in left-right asymmetry development and with such heart development, we use the zebrafish as a well-characterized model organism. In my PhD project, I perform small chemical compound screens by treating zebrafish embryos with drugs for which the molecular target is known. Analysis of heart looping and pancreas localization, as well as of blood flow and heart rates, help me to identify potential key factors in asymmetry as well as heart development. I elucidate the molecular and cellular mechanisms of receptors and signal molecules governing these processes. Moreover, since cilia appear to play an essential role during asymmetry development and since ciliopathies in general are becoming increasingly more important, I investigate the impact of the target molecules and other factors in cilia formation and function.

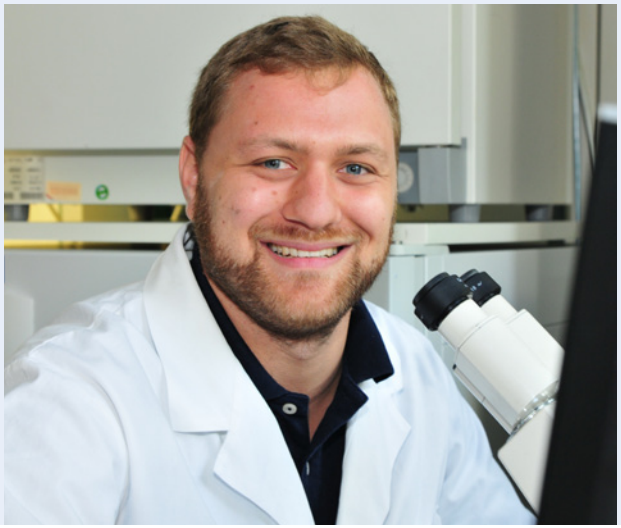
Molecular analysis of different repeat polymorphisms and novel mutations in amyotrophic lateral sclerosis (ALS)

ALS is a devastating human neurodegenerative disorder and the most common form of motor neuron disease. In a cooperation project conducted by the Institute of Human Genetics and the Department of Neurology at Ulm University with the Munich-based Helmholtz Institute and the Department of Human Genetics, we were able to determine the complete protein-coding genome sequence of more than 250 index patients with familial ALS by using high-throughput sequencing techniques. Our aim is to identify and understand novel potential disease-causing variants pointing to yet unknown ALS disease genes. Using this approach, two genes, whose mutations can trigger ALS, could be identified in 2014. The identification of *CHCHD10* and *TBK1* as ALS disease genes underlines the importance of mitochondrial damage or dysregulated autophagy in the pathogenesis of ALS. Using cellular models, we investigate the molecular functions of identified mutations with the aim of understanding signaling pathways or molecular networks that may be disrupted by the pathogenic mutation. Another approach of my work is the identification and molecular analysis of genetic modifiers acting as disease-modifying factors. Intermediate repeat expansions in genes containing specific repeat motifs have been identified as risk factors for ALS. Therefore, I am also working on a comprehensive, genome-wide study on polyglutamine repeat-containing genes in order to analyze ALS-modifying effects of specific repeat-length alleles.

priv.

Melanie Martin

I am in the ninth semester of my medical studies and a participant in the study program in Experimental Medicine at the Institute of Pathology.



Tobias Martin

I was born in 1989 in Ulm. I am currently working at the Institute of Pharmacology and Toxicology, Ulm University Medical Center, in the research group of Prof. Dr. Holger Barth. My PhD project is part of Project A4 of the CRC 1149 and is funded by the DFG. Since July 2015, I have been a member of the International Graduate School in Molecular Medicine Ulm.

Analysis of different SOCS1 mutation subtypes as a possible prognostic factor in diffuse large B-cell lymphoma (DLBCL) and characterization of DLBCL-cell lines

Diffuse large B-cell lymphoma is the most common type of non-Hodgkin lymphoma, accounting for up to 30-40% of all cases. This tumor entity is very heterogeneous considering its clinical and molecular aspects. In the current project, we want to investigate SOCS1 mutations in a cohort of 414 patients out of the RICOVER60 study. In this study, the standard CHOP therapy schema was compared with the additional CD20 antibody, rituximab. SOCS1 acts as an inhibiting protein within the JAK-STAT pathway and thus influences tumor cell proliferation. Our aim is to differentiate between mutational subtypes concerning prognostic value and treatment.
Besides we want to characterize and compare different cell lines with regard to create potential experimental models for cancer research.

Targeted pharmacological inhibition of Rho-/actin-dependent monocyte recruitment into the alveolar space after blunt chest trauma

The aim of Project A4 of the CRC 1149 is the establishment of cell type-selective bacterial protein toxins which specifically inhibit central regulators of chemotaxis, including Rho-GTPases and F-actin. My role within this project will be to investigate the effects of recombinant C3-toxins on the chemotaxis of monocytes and their differentiation into alveolar macrophages.
C3 toxins are monocyte-/macrophage-selective Rho-inhibitors. Rho-GTPases regulate actin cytoskeletal dynamics and various central cellular processes that include cytokinesis, phagocytosis, adhesion and migration. RhoA-activity is required for transendothelial migration of monocytes. Inhibition of Rho activity by C3 toxins, e.g. C3bot from *C. botulinum*, prevents migration of macrophage-like cells *in vitro*.
The effects of C3-toxins on chemotaxis of murine and human monocytic cell lines and primary human blood monocytes and their differentiation into macrophages will be analyzed.
In cooperation with the research group of Prof. Dr. Markus Huber-Lang, the effect of the most effective C3-toxin on the enhanced recruitment of alveolar macrophages will be investigated in a clinically relevant blunt chest trauma animal model. For efficient C3-delivery to the lungs, C3-toxin will be coupled to biocompatible, degradable albumin hydrogels in close collaboration with Prof. Dr. Tanja Weil.

Lisa Merthan

Born on 8 June1988 in Aalen. I am working in the WG Arnim in the Department of Neurology. Before I began my PhD at the International Graduate School in Molecular Medicine, I completed my bachelor's in Pharmaceutical Technologies and a master's in Biomedical Sciences at the University of Sigmaringen.

Patrick Meyer

Born on 7 January 1984 in El Paso, Texas. Currently, I am working in the Department of Dermatology and Allergic Diseases and am part of the International Graduate School in Molecular Medicine Ulm. I started my studies in Biology at the University of Kiel in northern Germany, where I still have my roots, and finished in 2011 with a diploma in Forensic and Molecular Biology. Since 2012, I have been pursuing my PhD in Ulm.

Characterization of the nuclear endocytosis protein PICALM in Alzheimer models

Amyloid plaques, which are composed of aggregated amyloid β (Aβ), is a pathological hallmark of Alzheimer's disease (AD). Aβ is a proteolytic fragment of amyloid precursor protein (APP). For the proteolysis of APP into Aβ, it must be internalized in the cell to the endosomes where enzymes cleave APP. The internalization will be started with an endocytosis. PICALM is a clathrin-mediated protein which is involved in the endocytosis. PICALM was identified by a genome-wide association study (GWAS) as a risk factor for AD. In previous studies, it could be shown that PICALM alters the APP trafficking and processing. Furthermore, the shuttling of PICALM into the nucleus has also been shown. Interestingly, it has not been proved that PICALM interacts with APP. To find a connection between APP and PICALM via these adaptors, my project therefore focuses on APP adaptor proteins. Here, I want to demonstrate an interaction between PICALM and adaptor proteins which are all involved in the neurobiological development and processing of APP. Next, I want to check the transcriptional regulation of PICALM in the presence of adaptor proteins and the transcription levels of the APP adaptors in cells with a knockout or overexpression of PICALM. As both APP adaptors and PICALM are nucleocytoplasmic shuttling proteins, I want to analyze whether these adaptors influence the shuttling properties of PICALM. Based on these results, I will be able to further understand the function of PICALM and its role in the pathogenesis of AD.

Systems biology of aging and age-related diseases

In my thesis, I try to shine some light on changes in molecular mechanisms and gene-expression patterns during aging and in age-related diseases. I am particularly interested in the differences found in the healing processes of acute and chronic wound healing during aging. For this, I am using human skin samples taken from healthy young and aged individuals as well as from donors with normal or chronically disturbed wound healing. Since my group could already show that senescent cells, through the secretion of detrimental factors, might have an impact on wound healing during aging, I am focusing my interest on senescence and the senescence-associated secretory phenotype (SASP). To study these, I am using full-genome microarrays to analyze gene-expression patterns in our skin samples and, additionally, collaborating with the Medical Systems Biology Group to develop in silico models (Boolean Networks) for the SASP. The data generated from microarrays and these networks can afterwards be combined to simulate different genetic modifications that might be used to block or enhance a previously monitored effect, and will give us the possibility of finding suitable targets for therapy and of validating these *in vitro*.

Tatjana Meyer

I was born in Munich in 1990. In 2009, I started my bachelor's in Biology at the Ludwig Maximilian University in Munich. In my master's studies, I focused on Medical Microbiology and completed my master's thesis on Helicobacter pylori at the Max von Pettenkofer Institute. In June 2015, I joined the lab of Dr. Krönke at Ulm University in the Department of Internal Medicine III as a PhD-student.

priv.

Christopher Meyer zu Reckendorf

Born in 1983 in Marburg, Germany, I studied Biology at Ulm University until June 2011 with my main subjects in Molecular Biology, Genetics, Pharmacology and Organic Chemistry. Currently, I am conducting my PhD thesis at the Institute of Physiological Chemistry and have participated in the International PhD Programme in Molecular Medicine since October 2011.

Functional characterization of the BRCA1-BRCA2-containg complex 3 (BRCC3) in myelodysplastic syndromes (MDS)

In my PhD thesis, I work on the functional characterization of the BRCA1-BRCA2-containing complex 3 (BRCC3) in the context of myelodysplastic syndromes (MDS), a clonal disorder of the bone marrow. BRCC3 is a deubiquitinating enzyme which participates in cleaving of Lys63-linked polyubiquitin chains and is also involved in DNA double-strand break repair. Recently, recurrent mutations in BRCC3 were detected in MDS. However, it is unclear how these mutations contribute to disease. Furthermore, BRCC3 has been shown to bind to CRBN, the target of lenalidomide, a drug with activity in MDS. In my thesis, I will investigate the role of mutated BRCC3 in MDS and its impact on lenalidomide treatment. Using a combined approach of proteomic, molecular biology and mouse experiments, we aim to identify downstream substrates of normal and mutated BRCC3 that are involved in the malignant transformation of hematopoietic stem cells. Results from this project may help to further define the role of altered ubiquitination in cancer and how it can be exploited for targeted therapy.

Identification and functional characterization of Serum Response Factor (SRF) cofactors in neurons

SRF is an ubiquitously expressed transcription factor that can be found in almost all cell types. SRF activity is regulated by the interaction with specific cofactors in order to drive diverse cellular responses to different stimuli. It has previously been shown that neuronal stimulation (e.g. by kainate) leads to an upregulation of SRF-dependent Immediate Early Genes such as *c-fos* or *Egr-1*. Nevertheless, up till now very little is known about the specific interaction of SRF with its cofactors and the remodeling of the transcription-regulating complex upon neuronal stimulation. A proteomic approach with mass spectrometric analysis of SRF-associated proteins, both before and after stimulation of a mouse brain with kainate, will shed some light on these complex processes. As a part of this project, the interaction of SRF with candidate proteins identified by mass spectrometry has to be confirmed by means of co-immunoprecipitation and western blotting. In a further step, the physiological role of those proteins has to be elucidated in neurons by analyzing their expression patterns before and after stimulation of the mouse brain (*in vivo*) or the neuronal cells (*in vitro*). Finally, the investigation of the effects of an overexpression or a silencing of those proteins in cultured wildtype neurons will reveal the importance of newly identified SRF cofactors for gene expression and neuronal morphology.

Viola Meyer-Pannwitt

I completed my bachelor's studies at the Bonn-Rhein-Sieg University of Applied Sciences and my master's studies at the University of Göttingen. Currently, I am working as a PhD student in the Department of Internal Medicine III within the Molecular Medicine program of the International Graduate School in Molecular Medicine Ulm.

Rashmi Mishra

Born in 1987, she received a B.Tech degree in Biotechnology (Genetic Engineering) from AAI-DU, India, and her M.Tech degree in Biotechnology from VIT University, India. She joined the PhD program in 2013 and works under the supervision of Prof. Dr Gilbert Weidinger at the Institute of Biochemistry and Molecular Biology.

The role of microenvironmental support in chronic lymphocytic leukemia

Chronic lymphocytic leukemia (CLL) is a type of cancer that effects white blood cells. It is the most common form of leukemia in the Western world and occurs mostly in elderly patients. Some patients experience a stable disease that does not require treatment whereas other patients have an aggressive form of this malignancy that necessitates early treatment. Despite recent advances in understanding the underlying molecular mechanisms of CLL, this cancer remains incurable.
The interaction of CLL cells with their microenvironment plays an important role in the pathophysiology of the disease and is therefore of interest to our laboratory. Our group has previously performed a gene-expression analysis of CLL cells co-cultured with stromal cells and could show a deregulation of signaling pathways involved in redox regulation. The aim of my thesis is to investigate affected pathways that are deregulated upon co-culture stimulation and are thus most likely responsible for prolonged survival and apoptosis resistance of CLL cells.

Molecular mechanisms regulating osteoblast dedifferentiation during zebrafish fin regeneration

During mammalian bone repair, new osteoblasts are derived from mesenchymal stem cells. In contrast, the zebrafish employs a unique and rare cellular process of dedifferentiation where mature osteoblasts are the precursors of regenerating bone.
This project aims to use the zebrafish caudal fin as a bone regeneration model to identify molecular regulators of cellular plasticity of bone cells. To achieve this, an *in vivo*, imaging-based and medium-throughput chemical screen of 2,000 biologically active small molecules has been designed. The identified candidate pathways will be verified using independent loss-of-function in particular transgenic-inducible overexpression of pathway inhibitors or knockdown of essential components using shRNA. To test cell-autonomous effects on osteoblasts, I will employ these tools in a tissue-specific manner using the TetON system. Based on this, future studies could strive to reprogram the mature osteoblasts to adapt the concept of dedifferentiation.

Agnieszka Maria Molisak

Born in 1986, I studied Molecular Biotechnology at the Gdansk University of Technology and graduated with an Engineering degree and a Master of Science. I am now working in the field of neurodegenerative diseases. My project is being conducted at the Boehringer Ingelheim-Ulm University BioCenter (BIU) and is part of a collaboration between the Institute of Physiological Chemistry at Ulm University and the Department of CNS Disease Research at Boehringer Ingelheim.

Haouraa Mostafa

Born on 15 July 1989, I studied Molecular Medicine in Ulm. The first time I joined a research lab was in March 2011 and, since that time, I have been in love with science and decided to stay in Ulm to finish my PhD.
Currently, I am in the second year of the PhD program and am working in the Department of Experimental Anesthesiology at Ulm University Hospital.

Contribution of mitochondrial-derived reactive oxygen species in neurodegenerative diseases

Clinically, mitochondrial oxidative stress has been demonstrated to be involved in progressive neurodegeneration in many diseases such as Parkinson's or LHON. Preclinically, the animal models used to study the role of reactive oxygen species (ROS) in neurodegeneration have lacked the slow disease progression seen in real human diseases. Many toxins exist that can induce ROS (e.g. MPTP), but the consequent neurodegeneration is very fast. One approach, which specifically induces mitochondrial ROS, has been constitutive deletion of the superoxide dismutase 2 (SOD2) gene. Unfortunately, this knockout is lethal, with pups living only about two weeks. The goal of this project is to develop an animal model that results in a slow increase in ROS and followed by a steady and progressive neurodegeneration in order to mimic as closely as possible the human disease state. Specifically, I have focused on the Cre-LoxP recombinase system to induce tissue-specific SOD2 loss following injection of an AAV1-CMV-Cre viral construct. This approach allows investigations of ROS-induced changes in the organ of choice and at any time during an animal's life. This system can also be applied in a primary cell culture so that the precise mechanism behind ROS-induced neuronal degeneration can be investigated. Combined, these two approaches provide the possibility for more comprehensive answers concerning how, when and why mitochondrial ROS induces neuronal death.

Immune recognition of glioblastoma multiforme, cellular and molecular patterns

Glioblastoma multiforme (GBM) is the most aggressive form of brain tumor. Due to the lack of immune sensitization by the tumor in the brain, there is an urgent need for a new therapy. My task is to examine the immune system of those patients before surgery. In whole blood, I was able to find an immune-suppressive environment. Furthermore, I found immune anomalies in GBM patients and that defined markers proved to be highly relevant for survival. For example, patients with a high amount of Natural Killer (NK) cells lived significantly longer compared to patients with low amounts. In order to sensitize cytotoxic cells against the tumor, we established 7 cell lines from primary tumor tissue. With a chromium release assay and caspase assays, we assessed the kill of the tumor.
I am trying to investigate the signaling cascade between the brain and the peripheral immune system. Therefore, I isolated microparticles and found miRNAs which enhance and inhibit tumor growth. This context supports the idea that either immune modulation by autologous NK cell therapy or interference into the signaling cascade may constitute a new therapeutic option.

Gabi Mroz

Born in 1992 in Tübigen, I have been a medical student at Ulm University since 2012. Because I am fascinated by the idea of understanding the human body to the smallest detail, I started my seventh semester at the Institute of Physiological Chemistry under the supervision of Professor Bernd Knöll in September 2015. The study program in Experimental Medicine gives me the opportunity to pursue a practical medical doctorate in a basic research field.

priv.

Phillipp Mueller

Born in 1987 in Pforzheim, he completed his bachelor's degree in Pharmaceutical Biotechnology at the Biberach University of Applied Sciences in 2012. After one semester at FH Weihenstephan (Munich), he changed to RWTH Aachen University and graduated in Molecular and Applied Biotechnology in 2015 (MSc). In May 2015, he registered for a PhD at the Institute of Applied Biotechnology in Biberach.

Clinically relevant behavioral disorders in Srf knockout mice

During my PhD scholarship, I want to examine a particular *Srf* knockout mouse strain which showed interesting behavioral anomalies in comparison to wild-type mice.
Besides regulating the turnover of the actin cytoskeleton, SRF (serum response factor) controls so-called "Immediate-Early Genes" (IEGs), such as *cfos, Egr1, Egr2* or *Bdnf*. Some of these can act as transcription factors themselves or have other direct effector functions. IEGs correspond to the first biological reaction in cells to a diverse range of stimuli and can therefore be used as a marker for cells activated in this way. One known event inducing the transcription of IEGs is acute or chronic stress. Preliminary tests in cooperation with the German Mouse Clinic (GMC) in Munich revealed that *Srf* knockout mice are hyperactive and seem to have a deviating stress response. Regarding our mouse model, the stress-induction of IEGs is of particular interest because *Srf* knockout mice lose their hyperactive traits after immobilization stress, whereas wild-type animals become more active. The main focus of my thesis lies in the interaction between SRF, IEGs and hormonal components of the acute stress response that could explain the different phenotype. Because stress and the physiological effects on the body play an essential role in the etiology of various human diseases, we hope to gain insight into the genetic susceptibility to stress and thus provide new targets for possible pharmacological treatments.

Glycosylation of recombinant proteins in *Escherichia coli*

Carbohydrates linked to proteins are important for the interaction between cells and molecules. For therapeutical proteins, the glycosylation pattern is a crucial parameter for stability and activity. Due to the lack of proper glycosylation of recombinant proteins in bacterial production systems, recombinant biopharmaceuticals are commonly produced in insect or mammalian cells. A bacterial expression system capable of glycosylation could enable a cheaper production of therapeutics. This research project is focused on the *O*-linked glycosylation of recombinantly expressed proteins. Both the granulocyte colony-stimulating factor G-CSF and a mucin-derived substrate will be tested as recombinant target proteins. The first step forward was the cloning and expression of a soluble and functional human GalNAc-T2 (polypeptide *N*-acetylgalactosaminyltransferase 2) in *E. coli*. This project will assess the activity of the glycosyltransferase *in vivo*. Ideally, the sugar substrate will also be produced in the bacterial cell without creating any negative effects on growth and product formation. The project will design and assemble sugar biosynthetic cassettes that combine the genes required for the production of the sugar substrate in the host strain with the recombinant glycosyltransferase GalNAc-T2 and the target proteins.
The project is supervised by Prof. Dr. Gaisser (Biberach University of Applied Sciences) and in close collaboration with the research team of Prof. Dr. Eikmanns (Ulm University).

Bastian Müller

I am 24 years old and currently live in Ulm. I was born in 1991 and grew up in Offenburg. After school, I wanted to study away from my hometown and so I applied for a place at Ulm University. I am in the tenth semester of my medical studies and researching my doctoral dissertation at the Institute of Pharmacology and Toxicology under the supervision of Prof. Dr. Holger Barth.

Janis Müller

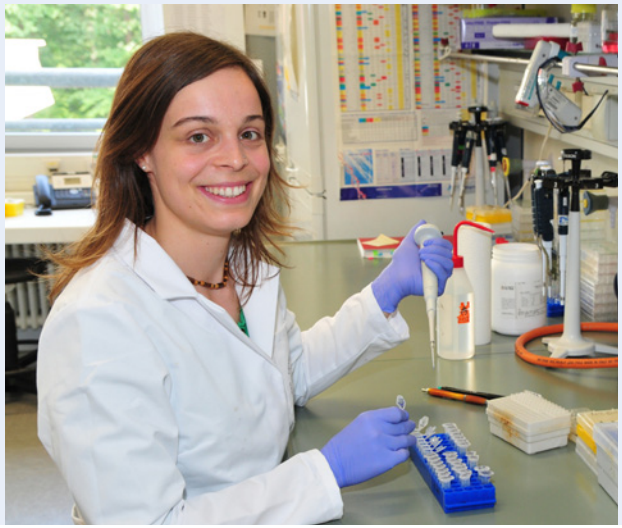
Born in Tübingen, I went to school in Frankfurt before returning south to pursue my fascination with the human body's physiology and to study Molecular Medicine at Ulm University. My studies in Ulm and Melbourne provided me with the research experience to understand how diseases and pathogens disturb life's beautiful balance and how research can contribute to restore homeostasis. I study at the Institute of Molecular Virology and am enrolled in the PhD Program of the IGradU.

Characterization of the inhibitory effects of bacitracin on the toxins A, B and CDT of *Clostridium difficile*

Clostridium difficile and its secreted exotoxins, A, B and CDT, are the main virulence factors linked to diarrhea and the more severe form of pseudomembranous colitis during antibiotic treatment. With the extensive and prolonged use of broad spectrum antibiotics during hospitalization, the frequency of such complications is rising dramatically. Today, the only therapeutic approach is to replace the causative agent by another, that is, an antibiotic that harms *Clostridium difficile*. Because more strains are resistant towards the few drugs normally used, there is a need for novel and direct toxin-inhibiting pharmacological strategies. Toxin A and B glycosylate and inactive small Rho-GTPases are important for intracellular signaling and stabilization of the aktin-cytoskeleton. On top, there are hypervirulent and severe subtypes producing the binary toxin CDT in addition to Toxin A and B. CDT ADP-ribosylates F-Aktin and so disrupts the balance between F-Aktin degradation and polymerization into a more degraded form. When researching new therapeutic drugs, we found that the known peptide-antibiotic, bacitracin which inhibits cell-wall synthesis in gram-positive bacteria, protects cultured cells from intoxication with purified toxin A, B and CDT. We characterize this new mechanism by monitoring the cell rounding after intoxication, either with each of the toxins alone or in combination. From this data, we produce dose-depending curves and calculated the IC_{50} values. Furthermore, we want to explore the suggested extracellular-specific mode of action and examine bacitracin in different experimental approaches.

The role of human semen and seminal amyloid in HIV infection

My research focuses on understanding the molecular basis of sexual transmission of HIV. Up to 85% of all new HIV infections occur following sexual intercourse, during which semen is the vector of transmission. Semen has been shown to enhance HIV infection rates and this activity has been attributed to the activity of seminal amyloids. My aim is to understand the molecular mechanisms by which semen amyloids promote HIV infection. Seminal amyloids interact strongly with viral and cellular membranes and thus capture viral particles and promote their attachment to cells. This ability to concentrate viruses not only increases infection rates but also influences viral stability, an effect that I discovered and characterized during my research for my PhD thesis. As a second part of my thesis, I want to understand how these amyloid-virus complexes interact with cells of the genital mucosa and how they can contribute to virus transmission and, thus, I analyze seminal amyloids in the presence of mucosal cells. Furthermore, I am interested in the fate of seminal amyloids after they have attached to cells, whether they are endocytosed or degraded, and what impact this has on infection enhancement. Finally, I am conducting studies into whether seminal amyloids may also enhance transmission of other viral pathogens and how the individual viral membrane proteins and their number can influence the outcome. Overall, I hope my research will increase our understanding of sexual transmission of HIV and lead to new HIV prevention strategies.



Marina Nagler

Born in 1987, she is performing her doctoral research study in the group for signal transduction under the supervision of Professor Dr. Meliha Karsak at the Institute of Physiological Chemistry and the Institute of Pharmacology and Toxicology. She has been a member of the PhD program of the International Graduate School in Molecular Medicine Ulm since October 2012.

Identification and characterization of cannabinoid CB2 receptor interaction partners

The revealing of signaling pathways and the functionality of cannabinoid CB2 receptor, a G protein-coupled receptor, are the focus of our research. In recent years, a vast number of research studies revealed the contribution of the endocannabinoid system to a multitude of disorders and I am convinced that the detailed understanding of the different parts of this system and its functional interaction is the basis for the pharmacological treatment of numerous human diseases. If nothing else, cannabinoid CB2 receptors are promising pharmacological targets in a range of human disorders, for example, in various cancer types and neurodegenerative diseases. For a detailed understanding of the function of CB2 receptor, we set out to search for putative interaction partners and/or modulating proteins. The aim of my work is to characterize the modulating effect of CB2 receptor on the dynein light chain protein, Tctex-1, and to study the biological relevance of the correlation of both proteins. For this approach, we are using molecular, biological and biochemical methods, such as, interaction studies via pulldown and co-immunoprecipitation approaches, co-localization studies by immunocytochemistry as well as expression experiments in different cells models.

Ester Nespoli

Born in Italy in 1988, I am enrolled in the International Graduate School in Molecular Medicine and am working in the Department of Child and Adolescent Psychiatry, Ulm University, and in the Department of the Central Nervous System at Boehringer Ingelheim Pharma.

The development of a juvenile animal model of Tourette Syndrome

The interest of my PhD thesis is to develop a juvenile animal model of Tourette Syndrome that could be used to test new drugs and to respond to the unmet needs of patients.
Tourette Syndrome is a tic syndrome which is often reported in movies as a funny syndrome where characters swear uncontrollably, but the reality is that Tourette is much more than this.
Unfortunately, it still remains a big puzzle to solve because there is little research in this field. I am a proud member of *TS-Eurotrain*, a group of 12 young and motivated researchers who are working hard together to shed new light on this complicated disorder. My task is to undertake the *in vivo* part of this work.

priv.

Sophia Neusser

Born in 1990, I am a medical student in the Department of Pediatrics and Adolescent Medicine and work in the group of PD Dr. Lüder Hinrich Meyer. I am also participating in the doctoral study program in Experimental Medicine (Promotionsprogramm Experimentelle Medizin).

The role of lysosomal cell death in T-ALL

Acute lymphoblastic leukemia constitutes 80% of all childhood leukemias. Although the prognosis is very good. 20% cannot be cured or suffer from relapses. Therefore, there is a constant need to develop new therapeutic strategies. Can lysosomal cell death be a therapeutic strategy for T-ALL? In the project, I work with the substances ABT-263, a BCL-2 inhibitor, and B10, a compound that induces lysosomal permeabilization. The aim of the study is to analyze whether there is a cooperative effect between B10 and ABT-263 to trigger lysosomal membrane permeabilization and cell death.

Julia Nissen

Born in 1992 in Stühlingen, Germany, she has been a medical student at Ulm University since 2012 and is currently working on her dissertation at the Institute of Human Genetics. She has been supported by the IGradU to participate in the study program in Experimental Medicine for medical students since July 2015.

Exome-sequencing-based identification of candidate genes for Möbius-Poland Syndrome

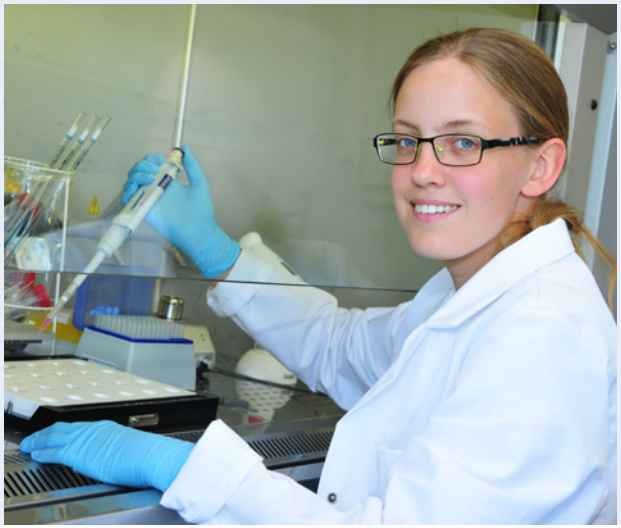
Individuals affected by Möbius-Poland Syndrome show an often bilateral facial and abducens nerve palsy (Möbius Syndrome) as well as a unilateral partial or complete absence of the great pectoralis muscle and deformation of the musculoskeletal system of the ipsilateral arm, most often syndaktyly (Poland Sequence).
So far, the cause of this phenotype is unknown. Genetic causes, as well as certain medication or complications during pregnancy, are currently being discussed in literature. To examine a possible genetic cause, DNA samples from five Möbius-Poland patients (three parent-case trios and two individual patients) have been collected and sequenced by next-generation sequencing. For this dissertation, the exome data of these patients are being screened under the assumption of a de novo mutation or autosomal recessive inheritance. Mutations in possible candidate genes will be confirmed through PCR analysis.

Verena Nold

Born in 1991, I studied Molecular Medicine at Ulm University. Since the summer of 2015, I have been enrolled as a Fast Track PhD student and work in the Department of Clinical & Biological Psychology in close collaboration with the Department of Clinical and Molecular Psychosomatics at Ulm University and the CNS Disease Research Department at Boehringer Ingelheim.

Biomolecular consequences of stress and trauma on the immune system

Chronic stress has been linked to several medical conditions such as major depression, post-traumatic stress disorder and cardiovascular diseases. Since the exposure to stress was found to increase, chronic stress is an increasing burden for physiological and psychological health. However, the underlying pathomechanisms of stress are not fully understood.
This PhD thesis investigates the effects of traumatic and chronic stress exposure on health by focusing on mitochondrial functioning and immune system activity. In various cohorts, I will assess psychoneuroimmunological changes induced by chronic stress exposure. The crosstalk between the immune system and the central nervous system (CNS) is evolutionarily anchored to ensure survival. In acute stressful situations, CNS-mediated stress responses lead to the secretion of immunosuppressive hormones. During acute inflammations, signaling molecules of the immune system interact with brain circuits regulating anxiety and vigilance. These tight interactions are beneficial but, with chronic stress exposure, the stress response systems will be activated continuously. Due to their susceptibility to these, the proper functioning of peripheral immune cells will be directly affected by chronic stress exposure.



Lara Nonnenmacher

Born 1990 in Heidelberg, Germany, she has been studying Medicine at Ulm University since 2010. As a medical student enrolled in the doctoral study program in Experimental Medicine (Promotionsprogramm Experimentelle Medizin), she has been working at the Institute of General Physiology since 2014.

The influence of inflammatory injury on the transport capacities of the airway epithelia

The airway epithelium separates the apical gaseous compartment from the basolateral liquid compartment. It is an important barrier against inhaled noxious substances. A thin fluid layer, the so-called apical surface layer, protects its apical surface. The volume and height of this liquid layer has to be tightly regulated by ion channels and water transport. Inflammatory damage can occur during pneumonia, asthma and COPD, and often results in an impaired regulation of the apical surface liquid volume and edema formation.
The aim of the present study is to examine how inflammatory injury of the lung epithelium influences the water transport through the epithelium and to identify inflammatory factors, such as cytokines, which impact transepithelial transport and barrier function.

Julia Josephine Ohmann

I was born in 1989 and currently a fifth year medical student at Ulm University. Since the beginning of 2015, I am a member of the study program in Experimental Medicine at the International Graduate School in Molecular Medicine. I work in the Traumalab under the direction of Prof. Dr. Huber-Lang at the Department for Orthopedic Trauma, Hand, Plastic and Reconstruction Surgery.

Najwa Ouali Alami

I was born in Italy in 1985 and graduated in Biology (Biology Applied to Research in Biomedicine) at the University of Milan. I joined the International Graduate School in Molecular Medicine in March 2015 after having been selected by Prof. Roselli to work as a PhD student in the Neurological Neuronal Network laboratory in the Department of Neurology at Ulm University.

The appearance and function of anaphylatoxins in the intestine, especially after polytrauma and during sepsis

C3 and C5 are two central components of the complement system, an essential part of innate immunity, and, upon activation, can be cleaved into the anaphylatoxins C3a and C5a, respectively. An excessive activation of the complement system with the generation of large amounts of C3a and C5a seems to play a detrimental role in tissue damage and systemic inflammatory responses, e.g. after polytrauma and during sepsis. In the intestine, the role of C3a and C5a is poorly understood. In my project, I analyze whether the epithelial cells of the intestine are able to generate C3a and C5a, and whether their intestinal generation is increased after polytrauma or during sepsis. Furthermore, I will determine what effects this activation might have on intestinal epithelial cell function and contribution to the dangerous gut-blood-barrier failure.

Investigation on Blood Spinal Cord Barrier (BSCB) and Blood Brain Barrier (BBB) disruption in ALS and neuroinflammation

Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disorder characterized by progressive paralysis due to the loss of primary and secondary motor neurons. Mutations in the Cu/Zn-superoxide dismutase (SOD1) gene are associated also with familial ALS and numerous hypotheses have been formulated to explain the non-cell autonomous mechanism of the disease, including impairment of the BSCB. The BBB and BSCB tightly regulate the blood and central nervous system molecular exchange required for normal neuronal function. Recently, it was postulated that the impairment of BSCB is one of the first pathological events. In transgenic mice carrying mutated SOD1 genes, a disrupted BSCB as well as decreased levels of tight junction proteins were detected. Moreover, ultrastructural changes due to the impairment lead to leakage, immune cells, IgG and albumin extravasation. Likewise, microglia activation and influx of immune cells have been reported but, whereas microglial activation is recognized as detrimental, the net contribution of the inflammatory response is debatable. The aim of the study is to achieve direct independent control of local permeability of the blood-brain barrier and microglia activation with minimal interference with other concomitant processes. Endothelial cell biology is dominated by several GPCR-dependent signaling and calcium channels. We propose to use GPCR-based and ion channel-based chemogenetics to control local signaling cascades in endothelial cells and microglia.

Noemi Pasquarelli

Born in 1989 in Berlin, I grew up in Rome and am now a Fast-Track PhD student in the Department of Neurology, Ulm University, and at Boehringer Ingelheim Pharma GmbH & Co KG., Biberach/Riß. Besides working in the lab, I enjoy life according to the principle of "Mens sana in corpore sano" and love doing sports, traveling around the world and cooking with friends.

Stefanie Pfaender

Born in 1984, she is a PhD student at the Institute for Anatomy and Cell Biology, and a member of the International Graduate School in Molecular Medicine at Ulm University. Her research focuses on zinc biology in stem cells and stem cell-derived somatic cells from healthy and autistic patients.

Pharmacological inhibition of monoacylglycerol lipase as a therapeutic strategy for neurodegenerative diseases

Cannabinoids and the endocannabinoid system are of growing interest for the development of therapeutic strategies against neurodegenerative diseases. This system consists of a) endocannabinoids such as anandamide and 2-arachidonoylglycerol (2-AG), b) cannabinoid receptors, and c) enzymes for the synthesis and degradation of endocannabinoids. It is especially the 2-AG-degrading enzyme monoacylglycerol lipase (MAGL) that represents a promising target since inhibition of MAGL may induce neuroprotective and anti-inflammatory effects by increasing 2-AG levels and decreasing arachidonic acid and prostaglandin levels.
The aim of my PhD project is to analyze the therapeutic potential of pharmacological MAGL inhibition in mouse models of amyotrophic lateral sclerosis (ALS) and Parkinson's disease (PD), two neurodegenerative disorders characterized by neuroinflammation and by the loss of motor neurons or dopaminergic neurons, respectively. This is done by treating an $SOD1^{G93A}$ mouse model of ALS and MPTP mouse models of PD with the MAGL inhibitor, KML29, and performing survival and phenotypic analyses. To further understand the potential and beneficial effects of MAGL inhibition, the mechanism underlying these effects is analyzed on a cellular and molecular level. With my PhD project, I hope to identify MAGL as a valuable target for the development of novel therapies against neurodegenerative diseases.

Zinc biology in the autism spectrum-associated disorder Phelan McDermid Syndrome

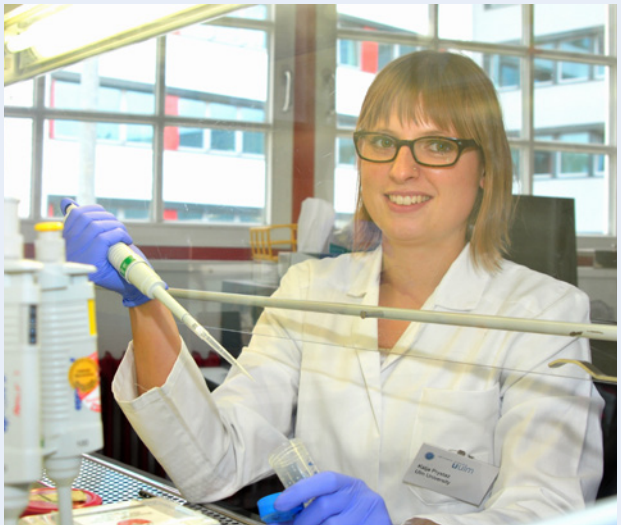
Zinc is one of the most prevalent metal ions in the brain and participates in such processes as neurogenesis, neuronal migration and differentiation, as well as synaptic plasticity and function, and thereby shapes brain development.
Phelan McDermid Syndrome (PMDS) is a neurodevelopmental disease characterized by infantile hypotonia, developmental delay, impaired speech, seizures and features of Autism Spectrum Disorders (ASDs). The major cause is a 22q13.3 deletion involving Shank3, a scaffolding protein that forms highly organized multimeric platforms at the postsynaptic density (PSD).
Given that recruitment and multimerization of soluble Shank3 at the PSD are zinc dependent, disruption of zinc homeostasis in PMDS patients might further enhance disease pathogenesis. Since zinc deficiency (ZD) has been reported repeatedly in ASDs, we first analyze a cohort of PMDS patients. The results point towards an increased incidence rate of ZD associated with the occurrence of certain symptoms. Using human iPS-derived cells from both patients and controls, we investigate the possible reasons for ZD. Screening the expression of zinc and other metal homeostasis proteins, our results indicate an impaired cellular zinc absorption in the gastrointestinal tract of PMDS patients. This leads us to the question whether consequences of this zinc deficiency can hint at a common mechanism in neurodevelopmental disorders accompanied by ZD and whether this non-genetic factor can be used to modulate the disease phenotype in the future.

Johannes Pospiech

Born in 1990 in Essen, he started studying Molecular Medicine at Ulm University in 2009. He graduated with a master's degree and joined the IGradU as a PhD student in the lab of Prof. Hartmut Geiger at the Institute of Molecular Medicine in 2014. In 2013, he received a Karl-Steinbuch-Stipendium (Karl Steinbuch Scholarship) from the MFG Stiftung Baden-Württemberg (MFG Foundation) to work on a computer model of the hematopoietic stem cell niche.

Wnt5a and hematopoietic stem cell aging: regulation and influence on expression and homing

Age-related loss of tissue function and development of age-related diseases are associated with aging of the stem cell compartment. Correspondingly, aging of hematopoietic stem cells (HSCs) results in impaired hematopoiesis in the elderly. While many molecular details of this mechanism are still under investigation, Wnt5a, a prototypical initiator of non-canonical Wnt signaling, has been shown to be strongly implicated in HSC aging. Indeed, we previously demonstrated that: (1) there is a profound increase in Wnt5a expression in old HSCs; (2) treatment of young HSCs with Wnt5a induces an aging-like phenotype; and (3) inhibition of Wnt5a expression in aged cells leads to rejuvenation of the hematopoietic system. The objective of my thesis is to investigate the regulation of Wnt5a expression and to examine whether it affects the expression profile and homing of HSCs. To address these questions, both NGS methods (RNA-Seq and Methylome data) and traditional assays will be applied.

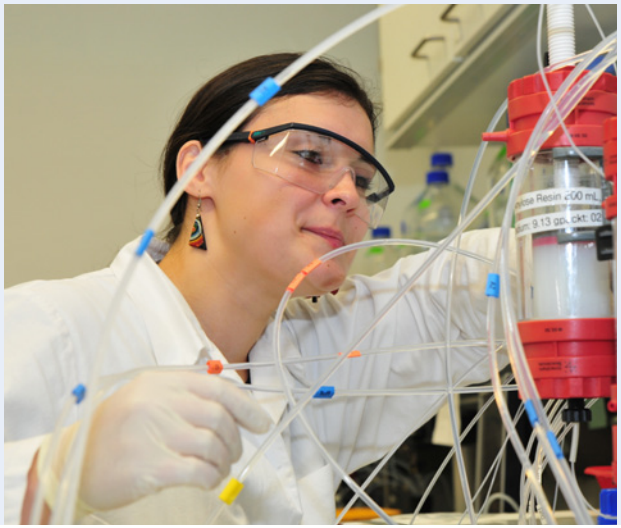


Katja Prystaz

Born in 1988, she studied Biology and started her PhD program at the IGradU in April 2014. She is currently working at the Institute of Orthopedic Research and Biomechanics where she is investigating the role of interleukins on fracture healing.

Mechanisms of interleukin-6 action in bone regeneration

Interleukin-6 (IL-6) is secreted by a variety of immune cells and modulates bone metabolism. IL-6 has different effects on osteoblasts, osteoclasts and chondrocytes, all of which participate during bone regeneration. The IL-6 effects on bone cells depend on the cell differentiation stage and IL-6 concentration. IL-6 is also considered to play an important role in bone healing. As reported in literature, IL-6 expression during fracture healing is biphasic. It peaks during the acute inflammatory phase and again during the bone repair phase of the fracture healing. Investigations of the mechanistic function of IL-6 in fracture healing are very limited. However, its significance has been indicated in several experiments with IL-6 knockout mice. One important drawback of these studies is that generalized IL-6 knockout leads to multiple dysfunctions which hamper specific clarification of IL-6 action. IL-6 signals are transmitted by two distinct mechanisms: classic signaling and trans-signaling. However, the role of these distinct pathways in different phases of bone regeneration is currently unclear. Here, we will study the impact of IL-6 classic and trans-signaling on the inflammatory, repair and remodelling phases of fracture healing. The results of our study will help to develop novel therapeutic approaches to improve bone healing in patients. The project has a strong translational character because modulators of IL-6 pathways are already in clinical trials for other inflammatory diseases.



Ioana Puscalau-Girtu

I was born in Romania in 1990 and completed my Pharmacy degree in 2014. I currently have a PhD position at the Institute of Protein Biochemistry and am in the International PhD Programme in Molecular Medicine of Ulm University.

Melanie Rall

I was born in 1988 in Ulm, Germany. In 2013, I graduated from my studies in Molecular Medicine at Ulm University and received my MSc degree. To complete my master's thesis, I spent six months at the Edinburgh Cancer Research Centre in Scotland. Afterwards, I started working in the Department of Obstetrics and Gynecology in the Section of Gynecological Oncology and joined the IGradU in October 2013.

Cellular mechanism of amyloid fibril formation

Amyloidoses are a group of diseases characterized by the deposition of abnormal fibrils which are derived from the aggregation of misfolded proteins. In systemic AA amyloidosis, these polypeptide aggregates affect multiple organs, including spleen, liver and kidneys, leading ultimately to patient death if left untreated. AA amyloid fibrils are derived from the acute phase protein serum amyloid A (SAA).

Further understanding of how amyloid protein aggregates form would be relevant not only for the treatment of patients that develop AA systemic amyloidosis (secondary to chronic or recurrent inflammatory diseases) but also for a broad range of related diseases, since AA amyloidosis is an outstanding model for studying protein misfolding diseases.

Taking advantage of the *in vitro* aggregation assays, the recombinant protein expression systems and the cell culture model of AA amyloid formation established previously in the Fändrich laboratory, I intend to further investigate the mechanism by which cells take up SAA, and the process of amyloid formation and deposition in the hope that this work will lead to a greater insight into the pathology and pathogenesis of AA amyloidosis.

DNA double-strand break repair in aging human hematopoietic cells

The stem cell theory of aging suggests that loss or dysfunction of stem cells causes failure of tissue homeostasis and so leads to aging of tissues and the organism. Moreover, there is evidence that age-related changes in the DNA-damage response limit stem cell survival and thus longevity. Since hematopoietic stem and progenitor cells (HSPC) are responsible for maintaining the hematopoietic system for a whole life time, they need to ensure genomic integrity and thus repair DNA damage, including DNA double-strand breaks (DSB), both efficiently and with high fidelity to sustain a functional stem cell population. As data on DSB repair in HSPC is scarce and obtained almost exclusively in murine models, I hope to contribute to a better understanding of DSB repair in human HSPC compared to mature peripheral blood lymphocytes (PBL) and how repair processes might change during aging. Thus, I comparatively analyze the capacity and quality of DSB repair in cycling human HSPC and PBL cultures derived from donors of varying age. In these cells, the activities of distinct repair pathways are measured via an EGFP-based reporter system to detect the repair of I-SceI-induced DSB. Furthermore, DSB induction and removal are monitored and DNA damage signaling analyzed to find cell-type and age-related differences. Then, the mechanisms underlying the observed changes in the DNA-damage response are elucidated in more detail and, ultimately, key experiments are also repeated in hematopoietic stem cells versus progenitor subpopulations.

Linda Raphel

Born in 1983, I am a student in the International PhD Programme in Molecular Medicine and a member of the Department of Internal Medicine II (Molecular Cardiology). Our lab is mainly focusing on the genetic and molecular networks of heart development and function. The long-term goal of our research is the development of new therapies for heart/muscle diseases.

Stephanie Nadine Reichel

I was born in 1989 in Ulm and started my PhD thesis in January 2014 at the Institute of Physiological Chemistry under the supervision of Prof. Dr. Thomas Wirth. In the summer semester of 2014, I entered the PhD program of the International Graduate School in Molecular Medicine and am expecting to sit my second intermediate examination during the Spring Meeting next year.

Tbx20 regulates cardiomyocyte proliferation in zebrafish

The molecular mechanisms underlying the development of the heart are poorly understood but are of immense clinical importance. In the search for novel regulators of cardiac development and disease, we isolated the mutant zebrafish *Weiches herz (whz)* in an ENU mutagenesis screen. *Whz* displays significantly reduced ventricular cardiomyocyte numbers. By positional cloning, we identified that *whz* harbors a missense mutation which leads to the loss of the original stop codon of the zebrafish t-box transcription factor 20 (*tbx20*) gene. Furthermore, we demonstrated that the *whz* phenotype is caused by the loss of Tbx20 function. We also analyzed cardiac differentiation and the rate of apoptosis in *whz* mutant hearts and found no alterations compared to wild types. However, when we checked for the proliferation rate of cardiomyocytes in *whz*, we found a significant reduction compared to wild-type littermates.
We now aim to understand the genetic and molecular mechanisms by which Tbx20 regulates the proliferation of embryonic cardiomyocytes. Furthermore, we will investigate the role of Tbx20 during heart regeneration in adult zebrafish.

The role of glia-specific modulation of NF-κB activation in traumatic brain injury

Traumatic brain injury (TBI) represents the leading cause of mortality and morbidity worldwide in children and young adults. The consequences of TBI in surviving people can lead to long-term or life-long physical, cognitive, emotional and behavioral impairments. A common aspect of the pathophysiology of TBI is the post-traumatic development of a neuroinflammatory response. The IKK2/NF-κB signaling pathway is a central regulator of a variety of cellular processes that include not only inflammation but also CNS-specific functions. There is increasing evidence that NF-κB activation in glia cells is part of the pathophysiology in TBI. However, the detailed cellular function of NF-κB in this context is not fully understood so far. We established mouse models which allow the modulation of the NF-κB pathway based on the expression of either constitutive active or dominant negative IKK2. We combine these neuroinflammation mouse models with a closed head injury (CHI) model in order to define the role of glia-specific NF-κB activation/inhibition on inflammatory and regenerating mechanisms as well as the consequences for the overall outcome of TBI. Post-traumatic analyses include behavioral tests and MRI analysis, histological and biochemical analyses, as well as the investigation of blood-brain barrier integrity and formation of acute edema. Additionally, for the spatiotemporal analysis of NF-κB activation in our CHI model, we use a transgenic reporter mouse line with NF-κB dependent eGFP expression.

Dominik Reim

I was born in 1988 and joined the International Graduate School in Molecular Medicine Ulm in June 2013 after finishing my master's degree in Molecular Medicine. I am in my final year as a PhD student at the Institute for Anatomy and Cell Biology under the supervision of Prof. T. Boeckers and Dr. Dr. M. Schmeisser.

Tanja Reisser

Born in 1987, she studied Pharmaceutical Biotechnology at Biberach University from 2008 to 2012 and continued her master's studies at Sigmaringen University. In December 2014, she started her PhD at Ulm University Medical Center in the Department of Pediatrics and Adolescent Medicine in the group of Gudrun Strauß. She became a member of the International Graduate School in September 2015.

Synaptic pathways in Shank-deficient mice

My PhD project focuses on Autism Spectrum Disorders (ASD). At the postsynapse of neurons, we find a highly organized structure, the postsynaptic density (PSD), which is important for synaptic signaling. The Shank proteins (Shank1, Shank2 and Shank3) are considered to be "master scaffolding proteins" at the PSD and thus play an important role in determining its structure and composition. Yet, each of the three *SHANK* genes has been associated with ASD in patients.
At our institute, we analyze different mouse models with genetic deletions in *Shank* genes. The detection of behavioral and molecular differences observed between our mouse models and wild-type mice will help to understand the impact and the precise role of the *SHANK* genes in ASD.
Since the Shank proteins are of major importance in the PSD, I am working on methods to biochemically fractionate subcellular compartments to obtain the PSDs of neuronal tissue. To compare different effects in several areas of the brain, the distinct brain regions are initially microscopically dissected. Therefore, we are able to analyze the purified PSDs of distinct brain areas without them being affected by other cell compartments. With this procedure, I am analyzing ASD-related signaling components for possible differences occurring in the PSDs of our mouse models and wild-type mice. In view of converging pathways, we hope to identify the precise modules and pathways affected by *SHANK* mutations which might serve as targets for pharmacological intervention in our mice and, eventually, in ASD patients.

The role of Th9 cells in graft-versus-host disease (GvHD) and the graft-versus-tumor (GvT) effect

Th9 cells are a recently defined subset of T-helper cells that has been identified by the potent production of interleukin-9 (IL-9). Given the pleiotropic functions of IL-9, Th9 cells fulfill physiological immune responses against melanoma and intestinal worms, and are further involved in immune-mediated diseases such as allergies and autoimmunity.
In the context of bone marrow transplantation and the development of GvHD, Th9-cell functions are largely unknown so far. GvHD is induced by the activation of donor-derived T cells against recipient histoincompatible antigens which are recognized as "foreign" structures that lead to life-threatening consequences for the transplant recipient. To study the *in vitro* and *in vivo* functions of Th9 cells and their role in the context of bone marrow transplantation, Th9 cells are generated *in vitro* from murine naïve CD4 T cells. The transplantation of murine Th9 cells, together with T cell-depleted bone marrow into irradiated mice, will reveal the role of Th9 cells in GvHD induction. Since the anti-tumor effect of allo-reactive donor T cells of the transplant against residual tumor cells of the recipient is desirable, e.g. in the treatment of leukemia and lymphoma, it is also of great interest if Th9 cells are able to induce an effective anti-tumor response.

Julia Richter

Born in 1986, she has been a member of the International Graduate School in Molecular Medicine Ulm since 2012 and works in the group of Prof. Knippschild in the Department of General and Visceral Surgery.

Andreas Riegger

Born in 1989, I started my studies in Chemistry in 2008 at Ulm University. In 2013, I received my MSc by working on "A Toolbox for Site-Specific Peptide and Protein Modification." For my PhD, I am synthesizing macromolecular antivirals at the Institute of Organic Chemistry III under the supervision of Prof. Tanja Weil. Inspired by the synergy between chemistry and medicine, I joined the IGradU in 2015.

Role and prognostic relevance of casein kinase 1δ in colorectal cancer

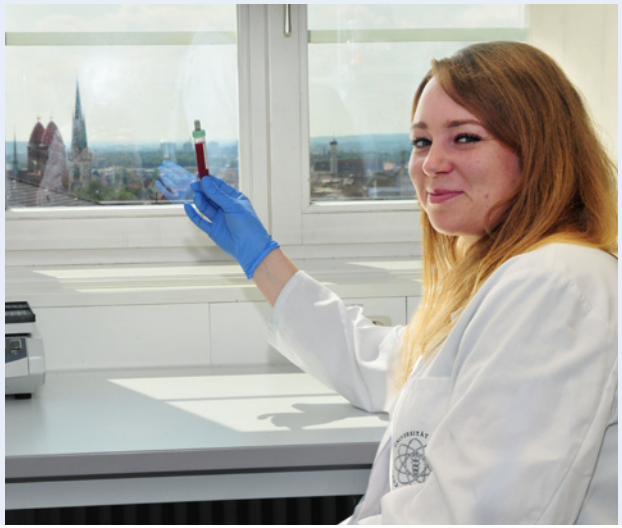
Colorectal cancer (CRC) is the fourth leading cause of cancer-related deaths worldwide. Although better therapies have resulted in prolonged median survival for patients, prognosis is still poor in advanced stages of the disease. Due to high apoptotic resistance and metastatic potential, conventional chemotherapy concepts are often ineffective and may be associated with severe side-effects. Therefore, research interests are focused on identifying new target molecules to serve as prognostic biomarkers in CRC and, ultimately, to facilitate development of new therapy concepts with enhanced selectivity, efficiency and reduced toxicity. Recently, interest in specifically targeting members of the casein kinase 1 (CK1) family has increased since CK1 isoforms are frequently deregulated in various tumor entities. So far, their potential as a prognostic biomarker and therapeutic drug target in the treatment of CRC has not been addressed in detail. Within the proposed project, new CK1 isoform-specific small molecule inhibitors have to be characterized for their inhibitory activity *in vitro* and in cell culture. Furthermore, the influence of CK1δ expression levels in colorectal tumor tissue on patient outcome as well as the effects of altered kinase activity on tumor growth have to be investigated to verify CK1δ as a potential drug target, thereby highlighting CK1 inhibition as a therapeutic concept in the treatment of CRC.

Synthesis of multivalent HIV infection inhibitors

As a trained chemist, I am interested in developing new synthetic tools for the synthesis of novel protein and peptide conjugates with biomedical applications. From a chemistry point of view, the design and synthesis of these bioactive macromolecules require reactions which can be conducted in a bioorthogonal fashion. These are chemical reactions that can occur within living systems, ideally without effecting biochemical processes or proteinogenic functions. We envision that these reactions facilitate an extensive engineering capacity for chemical functionalization of biomolecules to overcome hurdles and problems of peptidic drugs, both *in vitro* and *in vivo*.

As a prominent example, peptide-based HIV infection inhibitors, i.e. ALB (antiviral albumin fragment), have been described to prevent virus transduction through antagonistic binding of CXCR4 receptors. Intuitively, by adopting a multivalent and bioorthogonal chemical strategy, we aim to achieve a multiplicative inhibitory effect and to establish a semi-synthetic platform for antiviral therapeutics.

In this way, a broad variety of multivalent platforms, ranging from modified proteins to polymers or dendrimers, are synthesized and investigated for their inhibitory activity towards HIV infection. Additionally, these macromolecular scaffolds facilitate an extensive engineering capacity for chemical functionalization to further augment pharmacokinetic properties of these hybrid antivirals.



Lara Riehl

Born in 1988, she studied Molecular Biotechnology at the Technische Universität München (Technical University of Munich) until 2012 and afterwards started her PhD in the laboratory of Prof. Dr. C. Beltinger at the Department of Pediatrics and Adolescent Medicine. She is currently working on novel biomarkers for neuroblastoma with a special focus on mitochondrial DNA.

Novel blood biomarkers for neuroblastoma

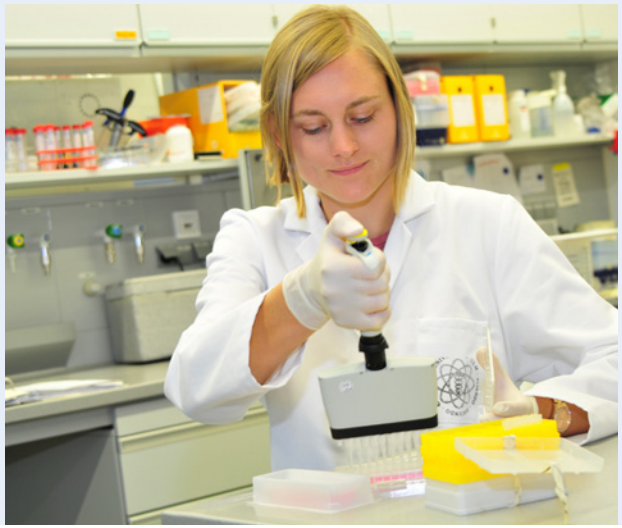
In neuroblastoma (NB), the most common extracranial solid tumor of childhood with a poor prognosis in advanced stages, more sensitive circulating biomarkers than the traditionally used catecholamines, LDH and ferritin, have to be found to facilitate initial diagnosis, assessment of therapy response and surveillance of tumor recurrence. Circulating mitochondrial (mt) tumor DNA is an appealing candidate biomarker due to its high mutational rate and copy number. The aim of this project is to discover new and clinically useful non-invasive biomarkers for NB, with a special emphasis on mt DNA variants. So far, a novel NB database, with over 120 consecutive samples of a total of 19 NB patients from Ulm University Medical Center and their complete imaging, pathology and clinical chemistry results over time, has been procured with data collection still ongoing. Furthermore, we show by massively parallel whole exome sequencing of normal, tumor and relapsed tumor tissues from 16 NB patients from the University Children's Hospital Essen that most NB harbor tumor-specific mt variants with increased frequency, a spatio-temporal evolution and a stable mutational signature during relapse. Tumor-specific mt variants may therefore constitute a new class of personalized biomarkers in NB.

Francesca Rizzo

I was born in 1987 and joined the Graduate School in Molecular Medicine in 2014 after finishing my degree in Medical Biotechnologies. My PhD project is a joint venture between the Institute for Anatomy and Cell Biology, the Department of Child and Adolescent Psychiatry, and Boehringer Ingelheim, and is under the supervision of Prof. A. Ludolph, Prof. T. Boeckers and Prof. B. Hengerer.

Investigation of the effect of psychotherapeutic drugs *in vivo* in a preclinical model of Tourette Syndrome (TS).

TS is characterized by vocal and motor tics with early onset and a high comorbidity rate with symptoms belonging to other neuropsychiatric diseases such as attention deficit/hyperactivity disorder (ADHD) and obsessive-compulsive behaviour (OCD). So far, no cure is available for patients and therapy is often limited to the management of severe tic or pathologic behaviors. My project focuses on establishing an animal model for TS in order to test the effect of two drugs belonging to the standard (neuroleptics) approach and a newly-proposed (glutamatergic modulators) therapeutic approach for tic-management, respectively. The animal model I use was published in 2013 in adult rats and, so far, it better fulfils the criteria of *face validity* (i.e. the ability of an animal model to reproduce patient symptoms). This model shows that tics are somatotropically organized rapidly after the intrastrital injection of a GABAA antagonist compound. Tics start as mild rapid movements of the finger, paw or limb and increase in intensity and frequency over time during the tic session. In order to better understand the mechanism of the tic generation process, juvenile control and SHR rats (an ADHD animal model) have been monitored during their developmental stages from puberty to early adulthood. Altogether, we analyze changes in the neurometabolite profile during brain development by using proton magnetic resonance spectroscopy *in vivo* and in their behavior in order to evaluate the effect of both drugs.



Annika Röcker

I was born in Ulm in 1990. After studying Life Sciences at the University of Konstanz, I applied for a PhD position at the Institute of Molecular Virology to participate in the Kooperatives Promotionskolleg Pharmazeutische Biotechnologie (Cooperative PhD Program in Pharmaceutical Biotechnology) offered jointly by Ulm University and the Biberach University of Applied Sciences. In April 2015, I joined the Graduate School and became a member of Prof. Dr. Jan Münch's group.

Sascha Rode

Born in 1989 in Germany, I studied Biochemistry and Molecular Biology at the University of Potsdam. During my master's thesis at the University of Pittsburgh, I focused on amyloid-forming peptides and proteins. Since 2014, I have been a member of the International PhD Programme in Molecular Medicine and work at the Institute of Molecular Virology at Ulm University under the supervision of Prof. Jan Münch.

Antiviral and anti-amyloid activity of small molecules and peptides

The attachment and binding of viruses such as HIV-1 to target cells require multiple interactions. Interestingly, the infection rate of HIV-1 is known to be significantly increased by the presence of seminal amyloid fibrils. We try to interfere with these mechanisms at several stages in order to reduce viral infection. Currently, I follow three ways to achieve this goal:

1. Many viral envelope proteins and amyloid fibrils possess heparin-binding domains. Therefore, a library of newly identified organic molecules, which are known to inhibit the interaction of proteins with cellular glycosaminoglycanes, is screened for antiviral and anti-amyloid activity.
2. Molecular chaperones are important agents in protein folding. The so-called BRICHOS domain is present in various proteins. The chaperone activity of this domain empowers it to inhibit Aß fibril formation and disaggregate these fibrils. We want to find out whether this chaperone also has an effect on seminal amyloid fibrils and/or HIV-1 infectivity.
3. Recently, the antiviral and anti-amyloid activities of a so-called molecular tweezer had been characterized by our group. This is an organic molecule which both inhibits the fibrillization of certain peptides and disaggregates pre-formed fibrils, thus antagonizing their infectivity-enhancing activity. Moreover, by destroying the viral membrane, it exerts a direct antiviral effect. By testing derivatives of this tweezer, we want to dissect the antiviral from the anti-amyloid mechanism.

Nanofibrils to target virus/host interaction and optimize gene transfer

My PhD project focuses on the interaction between nanofibrils, cells and viruses. It has been shown in recent years that amyloid fibrils in semen enhance infection rate of viruses, including HIV-1. This behavior was used to design and synthesize short peptides which quickly form amyloid fibrils and enhance viral infectivity based on the positive net charge. These synthesized fibrils are called nanofibrils.

To clarify the mechanism of viral infection enhancement, I use different high-resolution microscopy methods to obtain more details about the interaction of the cellular membrane and nanofibril/virus complexes, and the further internalization and degradation of the complexes by the cell.

The second project is focused on cellular restriction and sensing of nanofibril-mediated HIV-1 infection. So far, it is not known whether the presence of nanofibrils not only increases the overall infection rate but also the number of infections per cell. Multiple infections of a single cell might result in increased concentrations of incoming viral proteins, integrated proviruses and viral gene expression. In the case of seminal amyloid fibrils, this might help to overcome cellular restriction and enhance productive infection and successful viral transmission.

Determining whether nanofibrils allow multiple infections per cell is also relevant for nanofibrils as an increased copy number of the transduced gene could have beneficial or detrimental effects in gene transfer or therapy approaches.

Linda Röhner

I was born in Nürtingen in 1987. My bachelor's in Biology at Ulm University was focused on Molecular Biosciences. During my master's thesis, I investigated the functional relevance of microRNAs in AML at Ulm University Hospital. Since October 2015, I have been a PhD student in the lab of Dr. Krönke at Ulm University Hospital in the Department of Internal Medicine III.

Julian Roos

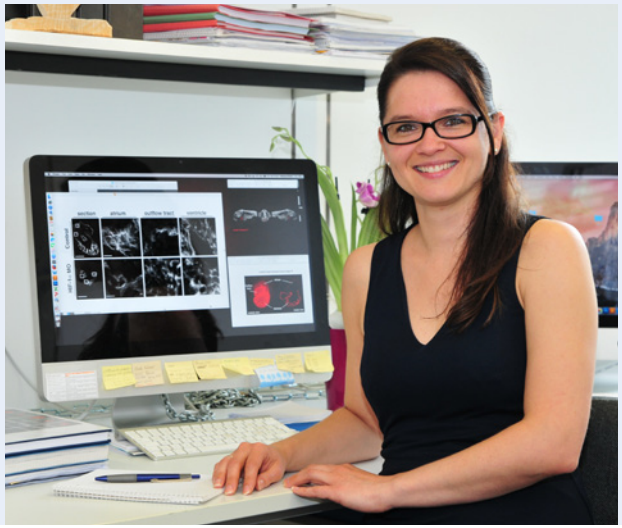
I was born in 1989 in the small Swabian city of Göppingen in Germany. I studied Molecular Medicine at Ulm University and now work in the Division of Pediatric Endocrinology and Diabetes (PEDU) in the Department of Pediatrics and Adolescent Medicine at Ulm University Medical Center. I am also enrolled in the International PhD Programme in Molecular Medicine.

The role of FAM46C mutations in the pathogenesis of multiple myeloma and their impact on lenalidomide sensitivity

In my PhD thesis, I investigate the role of FAM46C mutations in the pathogenesis of multiple myeloma, a genetically heterogeneous cancer of plasma cells, and their impact on lenalidomide sensitivity.
FAM46C is a protein of unknown function that is found to be mutated or deleted in multiple myeloma patients and is associated with impaired overall survival. However, it remains unclear how FAM46C mutations or deletions contribute to the progression of multiple myeloma. It has been shown that FAM46C binds to the CRBN-CRL4 E3 ubiquitin ligase, the primary target of lenalidomide, suggesting that mutations in FAM46C influence drug sensitivity.
My work includes the functional characterization of FAM46C and the contribution of mutated FAM46C to the development of multiple myeloma and to lenalidomide treatment. For this purpose, I will perform proteomic and molecular biological approaches as well as mouse studies.
Further understanding of the aberrant pathways in multiple myeloma and its consequences for drug activity have the potential to develop new therapeutic strategies for this disease.

Function of microRNAs in human adipocytes

Obesity leads to chronic low-grade inflammation within white adipose tissue. The increased production and secretion of pro-inflammatory cytokines promotes the development of insulin resistance and type 2 diabetes mellitus. Different miRNAs are known to serve as potent regulators of the human inflammatory response. Based on a previously performed miRNA array, we identified candidate miRNAs involved in adipose tissue inflammation. These candidates will be investigated in gain- and loss-of-function approaches to elucidate their biological role not only in the adipocyte inflammatory response, but also in the context of adipogenic differentiation, metabolism and adipokine secretion.
In addition, we aim to expand current knowledge on the possible mechanisms of miRNA secretion. The small oligonucleotides can be detected in body fluids and they have been proposed as biomarkers for several disease conditions. In obesity, adipose tissue is excessively enlarged and, therefore, adipocytes might provide the source of an altered circulating miRNA pattern. We aim to investigate the mechanisms of miRNA release in adipocytes.



Melanie Rothe

I studied Biology at the University of Würzburg. Since June 2012, I have been doing my PhD at the Institute of Biochemistry and Molecular Biology in the group of Professor Dr. Michael Kühl. I am part of the Tissue Homeostasis Joint PhD Program. This program is a cooperation between the Biocenter Oulu in Finland and the International Graduate School in Molecular Medicine Ulm.

Mónica Rubio Ayala

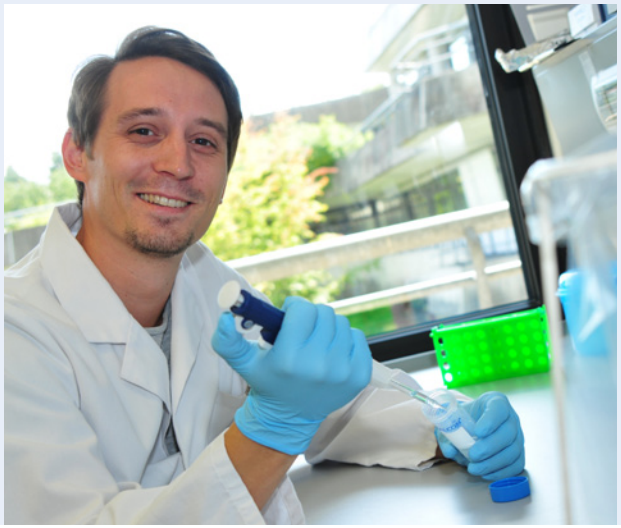
Born in 1988, she is doing her PhD at the Institute of Pharmacology of Natural Products and Clinical Pharmacology. Previously, she did her degree in Physics at the Complutense University of Madrid and spent one year abroad at the Technical University of Munich as well as completing her master's in Biophysics at the Autonomous University of Madrid. Her area of interest is magnetic nanoparticles in cell biology research.

Characterization of HIF-1α during heart development in *Xenopus laevis*

Congenital heart disease (CHD) is the most common type of major birth defect and this disease is characterized by defects in heart structure and function as well as defects in the great vessels. During mammalian development, the first functional organ is the heart and interference during cardiac developmental processes can lead to malformations of the heart.
It is known that the transcription factor hypoxia-inducible factor-1 (HIF-1) functions as a master regulator of oxygen homeostasis and triggers many cellular processes during embryogenesis. Studies by others have indicated that the α-subunit of the HIF-1 complex is required for cardiogenesis. However, the precise role of HIF-1α during early cardiac development is still unknown.
My main objective is to further characterize the role of HIF-1α by performing loss of function studies and to identify the underlying molecular mechanisms during early cardiac development by using *Xenopus laevis* as the model organism.

Development of new nanomaterials for the modulation of cell function

Although many current drugs interfere with the function of cellular receptors, nanoparticles possessing magnetic properties offer great opportunities for diagnostic and therapeutic application in a low-invasive environment. Nowadays, nanoparticles are used for imaging and drug delivery. Magnetic materials can be classified according to their response to a magnetic field. Among them, superparamagnetic nanoparticles exhibit outstanding characteristics which can be exploited in biomedicine. The aim of this project is to target the superparamagnetic nanoparticles to a specific receptor by using a protein as a linker. Once the superparamagnetic nanoparticles have been bound to the receptor, we apply a magnetic field. As a consequence, the nanoparticles will move in the direction of the magnetic field and cause a force in the receptor leading to its activation which will interfere with the signaling cascade. Furthermore, we want to use the cellular receptor as a switch which could be *on* or *off* in the presence or absence of a magnetic field. With this project, we expect to create biocompatible superparamagnetic nanoparticles which can be further used to induce changes in cellular behavior by activating or deactivating receptors on the surface of the cell membrane.



Steven Rudeck

Born in 1984, I am a student in the International PhD Programme in Molecular Medicine and a member of the Department of Internal Medicine II (Molecular Cardiology). Our lab is mainly focusing on the genetic and molecular networks of heart development and function. The long-term goal of our research is the development of new therapies for heart/muscle diseases.

Juliane Sachsenweger

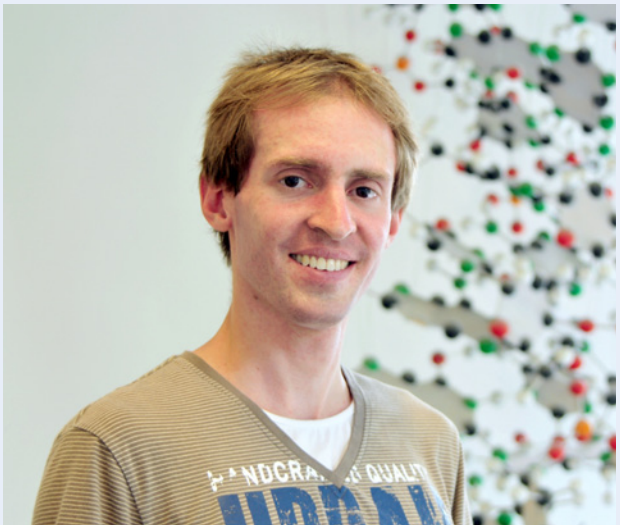
I was born in 1990 in Hoyerswerda, Germany. In 2013, I received my MSc in Molecular Life Sciences from the Friedrich Schiller University Jena. Before joining the IGradU, I worked at the Leibniz Institute on Aging in Jena. Since October 2014, I have been part of the IGradU and am working in the Section of Gynecological Oncology in the Department of Obstetrics and Gynecology.

The misfolded myosin response in health and disease

Assembly, maintenance and renewal of sarcomeric units require highly organized and balanced folding, transport, modification and degradation of sarcomeric proteins. However, mechanisms that regulate these fundamental processes are still poorly understood but of great clinical importance since many cardiac and skeletal muscle diseases are associated with defective sarcomerogenesis. To define novel genetic components of muscle myofibrillogenesis, we performed a forward genetic mutagenesis screen in zebrafish and isolated the recessive mutant *flatline (fla)*, which shows disturbed sarcomere assembly exclusively in heart and fast-twitch skeletal muscles. The *fla* mutant phenotype is based on a nonsense mutation within the SET- and MYND-domain-containing protein 1 gene (*smyd1*), which is a key player in processing sarcomeric myosin, and thereby in the orchestration of thick filament assembly. *Smyd1b*, which in mice is also known as *mBop*, is a candidate gene for heart muscle disease such as dilated cardiomyopathy (DCM) in humans. We screened DCM patients for *smyd1* mutations and found several variations that might cause DCM. Several key questions about the function of SMYD1 are part of this project, for example, the identification of SMYD1 methylation targets or the identification of new SMYD1 interaction partners.

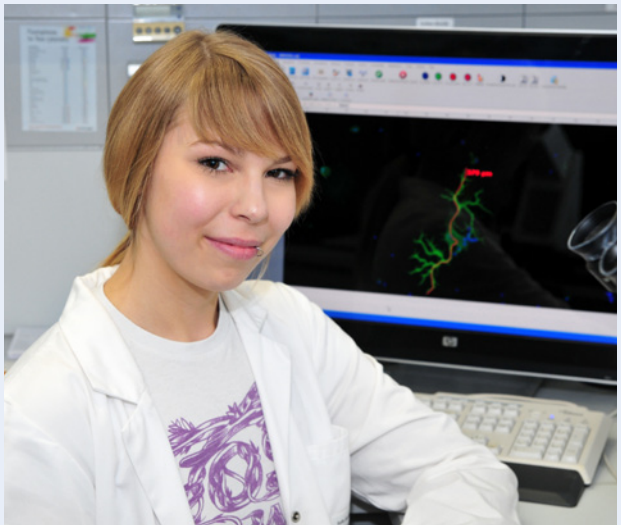
Molecular mechanisms leading to DNA damage response defects in patient cells carrying heterozygous mutations in the *PALB2* or *ABRAXAS* gene

Breast cancer is the most common cancer in women worldwide. Hereditary mutations in multiple genes of the DNA damage response/DNA double-strand break (DSB) repair pathways have been found to be associated with an increased breast cancer risk. In my studies, I focus on mutations in the breast cancer susceptibility genes, *PALB2* and *ABRAXAS*.
The c.1592Tdel Finnish *PALB2* founder mutation causes approximately a sixfold increase of breast cancer risk. Although the function of PALB2 in the regulation of homologous recombination is well understood, the effect of the *PALB2* c.1592Tdel mutation on DSB repair has not been sufficiently studied yet. The same holds true for the Finnish *ABRAXAS* c.1082G>A mutation. The objective of my project is therefore to elucidate the DSB repair activity of cells from patients displaying a hereditary breast cancer predisposition. In particular, the following aims are to be achieved:
1. Assessment of the DSB repair capacity/quality of *PALB2* c.1592Tdel and *ABRAXAS* c.1082G>A cells. Since these mutations represent a risk factor for breast cancer, it is particularly important to understand how they affect the genome integrity.
2. The comparison of the DSB repair capacity/quality of primary cells and cell lines from heterozygously mutated individuals between the Northern Finnish and other populations helps to assess the effect of different predisposing mutations and may improve the understanding of the impact of the genetic background.



Patrick Schäfer

I was born on 8 July 1989 in Reutlingen. Starting my studies in 2009, I did my bachelor's and master's in Molecular Medicine at Ulm University and then transferred directly to my PhD thesis via the Fast Track program in the autumn of 2013. Currently, I am completing my thesis in Experimental Neurology in the working group of Prof. von Arnim in a cooperation project with the Core Facility of Confocal and Multiphoton Microscopy.



Corinna Sophia Schilling

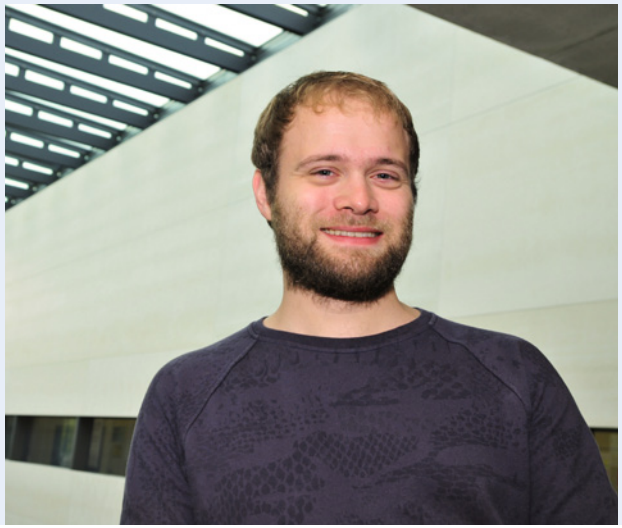
I was born on 27 November 1989 in Augsburg. My studies in Biology started in 2009 at Ulm University, where I graduated 2015 with a major in Molecular Biology and Neurobiology. My PhD program started in March 2015 at the Institute of Physiological Chemistry in the working group of Prof. Dr. Bernd Knöll. I chose to work here because the subject interested me and it seemed the perfect combination of my two majors.

High resolution monitoring of mitochondrial function by NADH FLIM in Alzheimer's disease

Alterations in cellular energy metabolism are prominent in a variety of pathologies. It is especially in neurodegenerative diseases such as Alzheimer's disease (AD) that mitochondrial dysfunction is one of the key factors occurring early in the pathology. The consequences are dramatic as reduced energy supply irresistibly leads to neuronal cell death. Interestingly, not all cells are affected but rather there is a selective vulnerability of cellular or even mitochondrial populations in the brain. Detection of the defective mitochondria is the basis for understanding the mechanism of the side-specific mitochondrial dysfunction and for a specific therapy of mitochondrial defects. However, current methodologies lack either functional relevance or spatial resolution.
In my PhD thesis, I establish and improve a novel microscopy-based method to functionally evaluate mitochondria.
Two-photon Fluorescence Lifetime Imaging Microscopy (FLIM) of NADH is marker free, exhibits a high spatial and temporal resolution, and even has the potential to be applied *in vivo*. It is based on changing portions of free to protein-bound NADH along metabolic alterations.
Thus, this method allows the detection of mitochondrial dysfunction on a cellular or even subcellular level. Being applied on primary neurons or organotypic hippocampal brain slices of Alzheimer's disease mouse models will provide new insights into AD-associated mitochondrial dysfunction and will pave the way for new therapeutical approaches.

Screening of bioactive molecules for regeneration of traumatic injuries of the facial nerve (*Nervus facialis*)

Traumatic injuries of the face have often a severe impact for the person affected. As injuries of the facial nerves are accompanied by facial paresis, patients therefore suffer not only from functional problems, such as impaired saliva production, but also from psychosocial stress.
In my thesis, I concentrate on analyzing bioactive molecules which can improve healing of injured peripheral nerves.
Therefore, in cooperation with the Institute of Organic Chemistry III, I will test so-called self-assembling peptides for their ability to improve neuron outgrowth *in vitro* in a high throughput screening.
Potential candidates of these *in vitro* screenings will be applied in a mouse model of a traumatic facial nerve injury. The grade of regeneration will be determined via histological examination and video-based analysis of whisker movement.

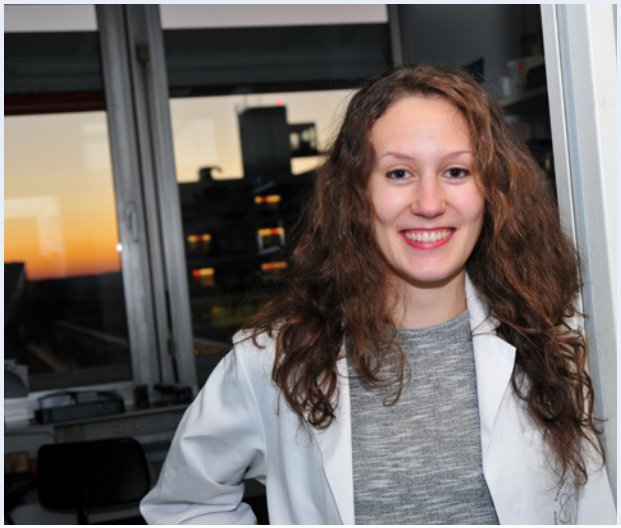


Florian Schmid

Born in 1987, I work as a research assistant in the core group in Medical Systems Biology and am a member of the International Graduate School in Molecular Medicine. My main research interests are machine learning, classification and other statistical methods for the analysis of high-throughput data.

Supervised analyses of genomic data

Modern high-throughput technologies, such as next generation sequencing, are able to measure several thousands of, for example, gene expression values of a biological sample. These techniques allow detailed snapshots of the activities in a tissue or cells. Because of the high dimensionality, this kind of data is very hard to analyze by hand.
An essential task is the development of statistical and computer-driven approaches for analyzing this data. The aim is to devise methods that have a high generalization performance and are interpretable at the same time. Supervised methods typically use a set of already categorized samples for training a model. The trained models can then be applied to distinguish between, for example, a tumor and inflammation. These diagnostic tools can support physicians in cases that are difficult to categorize. In this context, classification systems must be highly accurate and robust against measurement noise. Another aspect of supervised analyses is the interpretability of a model. If thousands of parameters are used, the interpretation of a model is very difficult. To allow an expert to generate a new hypothesis from such a model, it must be relatively easy and understandable in abstract terms. A knowledge-based selection of measurements is able to use available databases of abstract terms and associated signatures of measurements. By using these signatures, trained models are made interpretable for humans and allow the generation of new hypotheses.

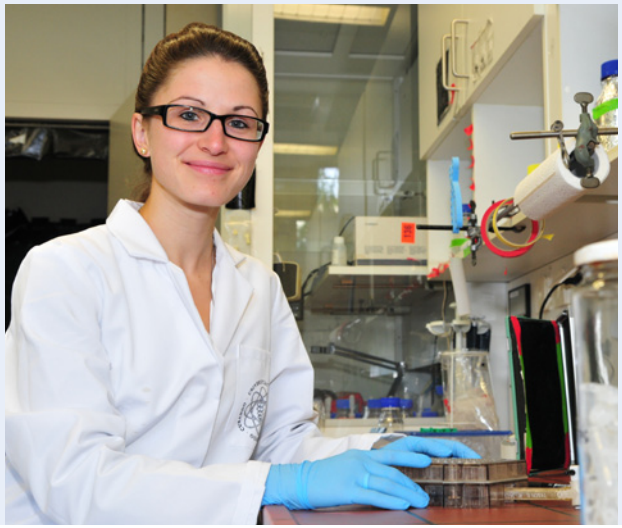


Teresa Schmid

I was born in 1993 and I am in the eighth semester of my studies in Human Medicine. At the moment, I am doing a doctorate at the Institute of Pathology and am pleased to be included in the doctoral study program in Experimental Medicine.

Characterization of U-RT 1 to develop a novel cell system for Richter syndrome to elucidate the clonal diversity and tumor evolution in B-CLL

Richter syndrome is defined as the development of chronic lymphocytic leukemia (CLL) into an aggressive lymphoma, most commonly diffuse large B-cell lymphoma (DLBCL). The majority of arising new neoplasms are clonally related to the underlying CLL. Richter syndrome occurs in approximately 2% to 10% of CLL patients during the course of their disease and is associated with a very poor outcome, especially when clonally related. The cell line, U-RT 1, was established from an EBV positive, male Caucasian CLL patient by tissue disintegration, long-term cell culture and subcloning by single-cell sorting. The patient showed several independent clonal events and a clonally related Richter syndrome, from which we isolated U-RT 1. My task was to characterize the cell line with several methods (immunohistochemistry, flow cytometry, mutational analysis, FISH, multicolor FISH and chromosome analysis). Now, I can apply different pharmacological inhibitors to U-RT 1 to determine the LC50 or IC50 with the aim of finding new therapeutical options for patients with Richter syndrome. Additionally, I examine formalin-fixed, paraffin-embedded samples of 13 patients with Richter syndrome.



Leonie Katharina Schnell

I was born in 1987. In 2007, I began studying Biology at Ulm University and received my master's degree in 2013. In the same year, I started my PhD project at the Institute of Pharmacology and Toxicology in the research group of Holger Barth. Since October 2013, I have been a member of the International Graduate School in Molecular Medicine Ulm.

Anna-Kristina Schroll

Born in Vienna in 1993, I decided to study Medicine in Germany after finishing school and then moved to Ulm in 2011. Currently, I am working on my doctoral dissertation in the group of Prof. Dr. H. Barth at the Institute of Pharmacology and Toxicology. I am in the study program in Experimental Medicine and received a scholarship from the International Graduate School in Molecular Medicine Ulm.

The role of host cell chaperones/PPIases during uptake of diphtheria toxin in mammalian cells

The aim of my DFG-funded project is to investigate the role that certain host cell factors play during the cellular uptake of the diphtheria toxin (DT). Consequently, I focus on a particular step of DT uptake, namely, the translocation of the enzymatic domain of the toxin (DTA) across the endosomal membrane into the host cell cytosol where the harmful enzymatic reaction takes place and leads to the clinical symptoms of the related disease of diphtheria. This translocation step is necessary for proper intoxication and is thought to be assisted by several factors of the host cell as in the case of, for example, the chaperone Hsp90. To investigate which factors play a role and in what way, I started by using different *in vitro* methods to determine the protein interactions between DTA and certain host cell factors. Therefore, I performed Dot blot analysis, co-precipitation, microscale thermophoresis (MST) and isothermal titration calorimetry (ITC) experiments. Furthermore, I perform intoxication experiments in the presence of specific pharmacological inhibitors of these factors to analyze their impact on DT intoxication of cells. The results of my thesis will contribute to a better understanding of the mode of action of the medically relevant diphtheria toxin and could lead to the development of novel pharmacological strategies to prevent intoxication of cells by DT and, consequently, the clinical symptoms of diphtheria.

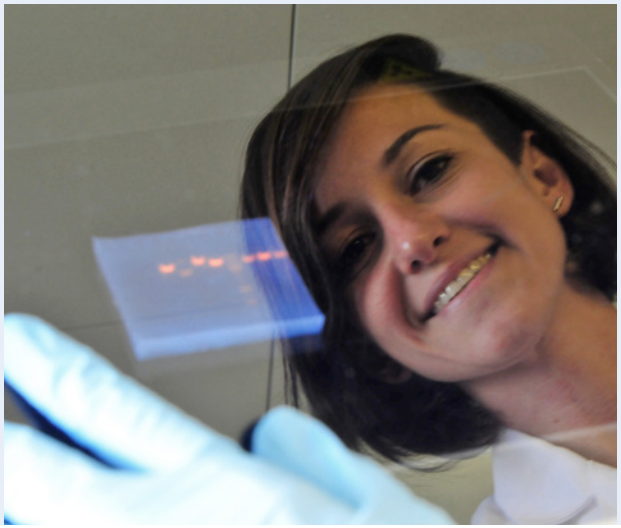
Characterization of the cytotoxic effects caused by the SubA subunit of Subtilase-cytotoxin produced by *Escherichia coli*

Subtilase cytotoxin (SubAB) is an AB_5-protein toxin produced by pathogenic Shiga-toxin expressing *E. coli strains*. The B_5 binding/translocation-subunit (SubB) mediates the uptake of SubAB into human target cells via receptor-mediated endocytosis. Consequently, the enzymatically active subunit (Sub A) reaches the endoplasmic reticulum (ER) where it cleaves the chaperone BiP/GRP78 and results in cell stress and caspase-dependent cell death. This process causes severe diseases such as hemolytic-uremic syndrome.

Recently, the Barth group unexpectedly discovered that SubA is able to cause cytotoxic effects in HeLa cells in the absence of SubB. Therefore, the goal of my work is to characterize this unknown mechanism and to determine whether SubA exploits a specific receptor to mediate its cytotoxic effects. Furthermore, we will test different cell-types regarding their sensitivity to SubA in order to find out if the cytotoxic effect of SubA is limited to epithelial cells.

Christine Schurr

I was born in 1986 in Schwäbisch Gmünd, Germany. Currently, I am working at the Institute of Physiological Chemistry, focusing on the role of neuroinflammation in the onset and progression of neurodegenerative diseases under the supervision of Prof. Dr. Thomas Wirth. I am expecting to finish my PhD at the International Graduate School in Molecular Medicine in autumn 2016.



Julia Segert

Born in 1984, I am a student in the International PhD Programme in Molecular Medicine and a member of the Department of Internal Medicine II (Molecular Cardiology). Our lab is mainly focusing on the genetic and molecular networks of heart development and function. The long-term goal of our research is the development of new therapies for heart/muscle diseases.

The role of neuroinflammation in the onset and progression of neurodegenerative diseases

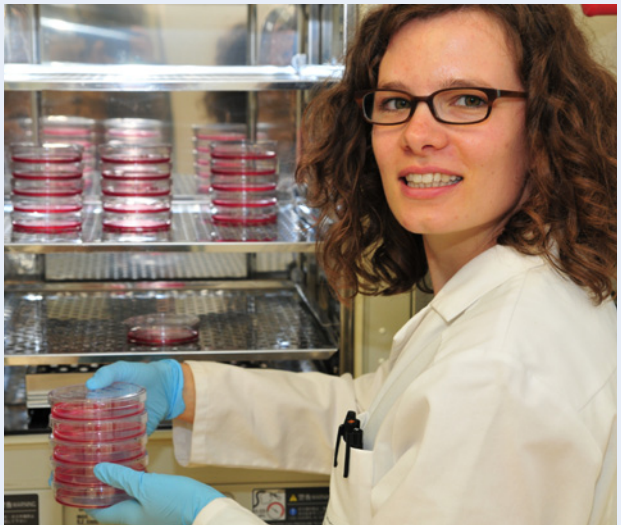
Neuroinflammation contributes to the development and progression of different neurodegenerative and auto-inflammatory diseases such as Amyotrophic Lateral Sclerosis (ALS) and Multiple Sclerosis (MS). However, the exact role of neuroinflammation in these diseases is not well understood and this is in part due to the lack of suitable animal models. Therefore, we started to establish novel mouse models that either combine the well-characterized ALS animal model SOD1-G93A or a MS model named TCR-2D2 with a model of conditional neuroinflammation. The latter model is a gain-of-function approach based on the astrocyte-specific expression of a constitutively active allele of human IKK2 using the tet-System. With this model, it is possible to induce neuroinflammation (via the NF-κB pathway) at any given point of time in the context of ALS or MS.
Using these combined models, we want to characterize the exact patho-physiological function of neuroinflammation in ALS and/or MS, and to identify a possible alteration of disease onset and/or progression. Motoric behavioral tests, together with histological and biochemical analyses, will be used to identify and characterize the phenotypes of the animals. It is hoped that this research will help to develop a strategy against ALS and/or MS.

Loss of Trap230/Med12 leads to defective AVC patterning in zebrafish

The molecular mechanism essential for accurate cardiac valve formation involves complex interactions among several signaling molecules and transcription factors (TF) which need to be regulated and controlled. Therefore, the Mediator Complex (MC) is an important multisubunit machinery for gene transcription, especially for the tissue-specific fine-tuning of transcriptional gene regulation. To analyze the signaling pathways involved in atrioventricular canal (AVC) patterning and, furthermore, in heart valve development, I am characterizing the zebrafish mutant, *trapped*, which has a nonfunctional MC kinase module subunit Trap230/Med12 (Med12). This mutation leads to a severe developmental heart impairment in zebrafish that results in a complete loss of heart valve structures. Whereas initial heart chamber formation appears normal in Med12-deficient embryos, further heart specification, such as AVC formation, is defective.
Less is known about Med12 function and its relevance during embryonic cardiogenesis. To gain a deeper understanding of the complex molecular signaling that induces heart valve development, my PhD project focuses on the role of MC kinase module subunit Med12 during AVC patterning. Preliminary results suggest that MC kinase module, including Med12, has a co-activating function for diverse TF to initiate AVC valve formation. Without Med12, specific TF are not activated and, therefore, AVC patterning is inhibited. At present, I want to elucidate which molecular pathways are affected by Med12 and if the kinase module directly phosphorylates the expected target TF to induce activity in AVC development.

Franziska Anna Seigfried

Born in 1986 in Heidenheim an der Brenz, I studied Biotechnology at the Technical University of Berlin and at Dongseo University in South Korea. Since 2013, I have been working on my PhD project on X. laevis development at the Institute of Biochemistry and Molecular Biology in the Kühl lab. I am a student in the Joint PhD Programme in Tissue Homeostasis offered by Ulm University in cooperation with the University of Oulu. I am also one of the few mothers currently studying at the Graduate School.



Katharina Senger

I am 27 years old and started my PhD at the end of 2013 at the Institute of Molecular Medicine in the lab of Hartmut Geiger. Since our lab is working on aging, I am currently a student in the CEMMA program.
In our lab, we are doing basic research in the field of hematopoietic stem cell (HSC) aging to elucidate and interfere with factors or pathways that are involved in aging and the decline of HSC function.

The role of Frizzled 3 and its target genes during *Xenopus laevis* development

During embryonic development, organogenesis is driven by growth factors such as Wnt proteins (Wingless-type MMTV integration site family member). Wnt ligands bind to Fzd (Frizzled) receptors and, consequently, activate different intracellular signaling pathways.
The Fzd3 receptor is known to influence organogenesis via its direct target gene *alcam* (activated leukocyte cell adhesion molecule). Part of the 5' untranslated region of *alcam*, which features two Pax2 (Paired box gene 2) and seven ATF2 (Activating transcription factor 2)-binding sites, has been found to trigger the expression of the *alcam* protein (Cizelsky et al., Development, 2014). The exact mechanism of gene activation, however, is so far not understood. My aim is to further characterize the promoter region of *alcam* in order to elucidate the mechanism of *alcam* expression.
In addition, I study the role of *alcam* during organogenesis in more detail by characterizing the function of identified *alcam* interaction partners using antisense strategies in *Xenopus laevis*.

Role of septins in hematopoietic stem cell aging

The functional decline of the hematopoietic system that is seen during aging has been linked to aging of HSCs. We have previously shown that the activity of the small RhoGTPase Cdc42 is increased in aged HSCs and that elevated activity is linked to a loss of polarity of specific proteins in aged HSCs. Pharmacological inhibition of Cdc42 activity restores the frequency of polarized aged HSCs to levels similar to young HSCs and rejuvenates their function.
Protein polarity in cells is organized and maintained by cytoskeletal proteins. My project is focusing on a family of cytoskeletal proteins called septins. Septins are well described in yeast, where they serve as diffusion barrier maintaining cell-fate determinants in the appropriate cell during budding. However, their function in mammals and, more precisely, in the hematopoietic system is largely unclear. It was previously shown that septins act downstream of Cdc42 via effector proteins called borgs in mammalian cell lines. Our hypothesis is that septins establish and maintain protein polarity in HSCs which is lost upon aging and that this function is regulated by Cdc42 activity via borg proteins.

Dilan Gün Serdar Sarialioglu

I was born in Istanbul in 1989. I completed my bachelor's degree in Molecular Biology and Genetics at Istanbul Technical University. In my master's thesis, I studied the effects of immunomodulatory drugs on transduced mouse multiple myeloma cell line at Ulm University in Dr. med. Jan Krönke's lab and am doing my PhD project in the same lab. I joined the International Graduate School in Molecular Medicine in the winter semester of 2015.

Claudia Soi

Born in 1987, she is doing her PhD under the supervision of Prof. Stefan Britsch at the Institute of Molecular and Cellular Anatomy. She joined the International Graduate School in Molecular Medicine in the spring of 2014.

Establishing a lenalidomide-sensitive mouse multiple myeloma model

Lenalidomide and its analogs, which are also known as Immunomodulatory Drugs (IMiDs), show remarkable efficacy in the treatment of multiple myeloma. It has been demonstrated that IMiDs bind to CRBN, which is a substrate adaptor of the CRL4-CRBN E3 ubiquitin ligase complex. IMiDs modulate CRBN's substrate specificity to recognize the two transcription factors, Ikaros (IKZF1) and Aiolos (IKZF3), and cause their ubiquitination and subsequent proteosomal degradation. Decreased protein levels of IKZF1 and IKZF3 have been shown to inhibit proliferation of multiple myeloma cells. However, mouse cells are resistant to these drugs and prevent studies of IMiDs in mice. The finding that this resistance is caused by a single amino acid difference (isoleucin to valine at position 391) between mouse and human CRBN protein raises the possibility of overcoming this resistance. The main task of this project is to establish a lenalidomide-sensitive mouse model for multiple myeloma. Our purpose is to confirm that mouse cells become sensitive to lenalidomide treatment via expressing either human CRBN or mouse CRBN protein with mutation I391V. The initial focus of the experiments is to validate degradation of IKZF1 and IKZF3 transcription factors as a consequence of IMiD treatment and to verify that proliferation of human CRBN or mCrbn^{I391V}-expressing mouse cells is inhibited by lenalidomide and other IMiDs. This mouse model will allow *in vivo* mouse studies, such as validation of combination therapies of lenalidomide and other drugs, dosage adjustments, and drug resistance mechanisms in multiple myeloma.

The role of Bcl11b in hippocampal mossy fiber development.

The hippocampus, consisting of the dentate gyrus, the cornu ammonis and subiculum, plays an important role in spatial memory and learning. The major gateway for information to the hippocampus is the dentate gyrus. The dentate gyrus receives inputs from the entorhinal cortex and then projects its axons, the mossy fibers, to the dendrites of the pyramidal cells of the cornu ammonis region 3 (CA3). The transcription factor B-cell CLL/lymphoma 11b (Bcl11b), a zinc finger protein, is expressed in the neocortex, striatum and hippocampus. Previously, it was shown that Bcl11b is essential for the development of the dentate gyrus (Simon et al., 2012). The deletion of Bcl11b caused a reduction of progenitor cell proliferation and differentiation as well as impairment of mossy fiber development, resulting in learning and memory deficiencies. The molecular mechanisms of mossy fiber development are still unknown. The aim of my project is to study the role of Bcl11b in mossy fiber development.

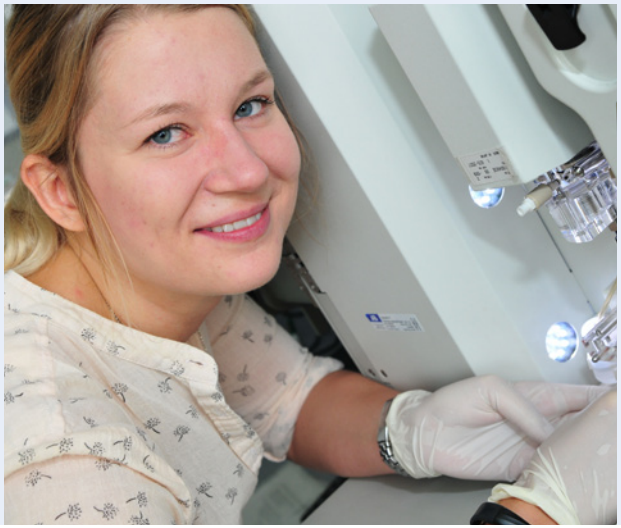
priv.

Aynur Sönmez

Born in 1991, I am neuroscientist from the beautiful Franconian town of Bamberg. Since the winter term of 2015, I have been a member of the International Graduate School in Molecular Medicine Ulm at the Institute of Applied Physiology and in the Research Training Group, CEMMA.

Dissecting metabolic factors controlling neuronal survival in health and neurodegenerative diseases

The aim of my PhD project is to investigate the mechanisms of neurodegeneration by focusing on dysregulation of neuronal activity and protein synthesis in Parkinson's disease and Huntington's disease. Dysregulated protein synthesis is common to several neurodegenerative disorders, but its neuroprotective/neurotoxic impact is still unclear. My project will include the analysis of translated mRNAs in specific neuronal populations affected in these diseases in order to identify novel factors that might modify the disease course at early stages. Ultimately, I will test the role of candidate genes differentially translated in health and diseases in neuronal activity and survival by loss/gain-of-function mutations in cellular and mouse models.
Metabolic and adaptive changes occurring before neurodegeneration could help to explain selective vulnerability of particular neurons in both diseases.



Nadine Sowada

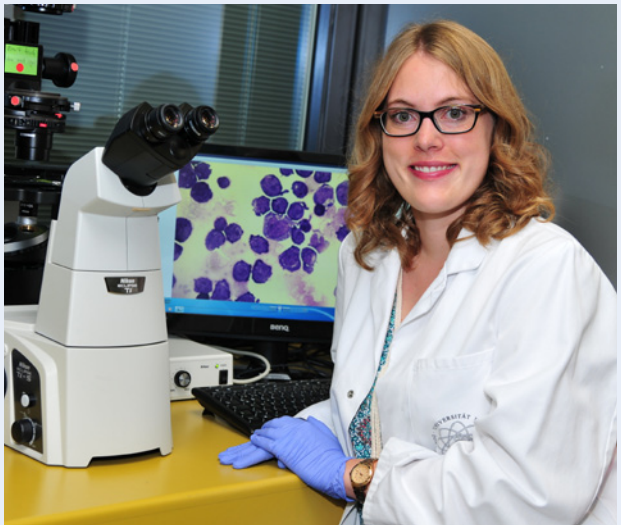
Born in 1984, she graduated in Biology at Ulm University. After finishing her diploma thesis, she joined the International PhD Programme in Molecular Medicine at Ulm in 2012. She is working in the lab of Prof. Christian Kubisch at the Institute of Human Genetics.

Functional involvement of the monogenic Parkinson's disease gene *VPS35* in heavy metal homeostasis.

Parkinson's disease (PD) is the second most common neurodegenerative disorder. In 2011, a *VPS35* missense mutation was found in independent PD patients of different families. The mutation leads to the exchange of aspartate to asparagine at position 620 (D620N) and shows an autosomal dominant inheritance. The amino acid D620 is highly conserved among species, including the budding yeast, *Saccharomyces cerevisiae*, which allows us to investigate the consequences of this mutation in the yeast ortholog. Vps35p is a component of the retromer. The retromer associates with endosomes and mediates vesicle transport from endosomes to the trans-Golgi network. Heavy metals are known risk factors of PD and, moreover, molecular and genetic interactions between PD genes and heavy metals have been shown in previous studies. I want to analyze the putative role of VPS35p in HM homeostasis in yeast.

Anna Katharina Speidel

Born in 1986, she studied Biochemistry at the University of Tübingen. After having written her diploma thesis in Lund, Sweden, she is now a PhD student at Boehringer Ingelheim GmbH & Co KG in its Department of CNS Diseases Research. Additionally, Anna is enrolled in the International Graduate School in Molecular Medicine and is kindly supported by the Institute of Pharmacology and Toxicology.



Nadine Sperb

I was born in 1989 in Villingen-Schwenningen. After studying Molecular Medicine at Ulm University, I joined the PhD program of the International Graduate School. Currently, I am working in Dr. Florian Kuchenbauer's group at the Department of Internal Medicine III.

iPSC-derived cell culture models to study neuropsychiatric and neurodegenerative diseases

Both neuropsychiatric and neurodegenerative diseases are gaining increasing attention in our society. However, the underlying causes have not been fully elucidated and adequate treatment is an unmet medical need.

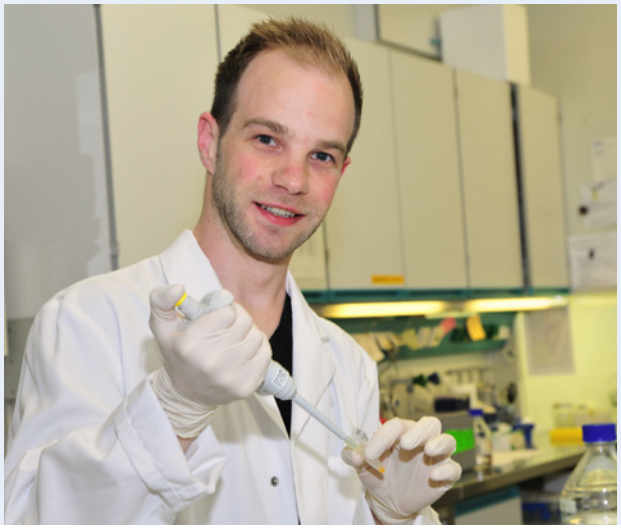
The discovery that somatic cells can be reprogrammed, yielding induced pluripotent stem cells (iPS cells), has caused a big leap forward in disease research. These cells, displaying similar properties as embryonic stem cells (ES cells), can be used to create patient-specific cell culture models to investigate possible disease mechanisms. Since variability in the genetic and epigenetic state of iPS cell lines might have a confounding effect, isogenic lines are required to study effects of disease-related gene mutations. In this project, the three major genome editing techniques, that is, zinc finger nucleases (ZFN), transcription activator-like effector nucleases (TALEN) and clustered regularly interspaced short palindromic repeats (CRISPR), are used and efficiencies are compared.

Generated cell lines harboring disease-relevant gene mutations are then used to establish cell culture models consisting of midbrain dopaminergic neurons and cortical glutamatergic projection neurons, which are cell types of relevance in both neuropsychiatric and neurodegenerative diseases. Since dysregulation of immune cells may be a cofactor in the pathophysiology of related disorders, iPS cells are additionally differentiated into monocytes/macrophages. Having evidence of correct cell identity and function, these models are used to study disease-related pathological mechanisms.

Modulating myeloid hematopoiesis through exosomes and miRNAs

Exosomes or, more generally, extracellular vesicles (EVs) are small membrane vesicles which eukaryotic cells secrete into their extracellular environment. Exosomes are 50 to 150 nm in size and are generated via an endocytic pathway. They carry signals, including proteins, mRNAs, microRNAs (miRNAs) and DNA, within or at their limiting membrane and provide a mechanism by which cells can exchange more complex information than previously thought. This long-distance transfer of genetic material is discussed as a mechanism of intercellular communication and is thought to play an essential role in physiological and pathological processes. Uptake of exosomes can manipulate the local and systemic environment to aid in cancer growth and dissemination. While exosomes have been mainly studied in solid tumors, only little is known about their role in hematologic malignancies.

This project aims to investigate how exosomes from leukemic entities contribute to the malignant transformation of the hematopoietic system by inhibiting myeloid differentiation. We also aim to characterize exosomes from different leukemic cell lines by proteomics and miRNA analysis. Furthermore, we want to identify (exosomal) miRNAs that are able to modulate differentiation and to functionally study them in the Hoxa9-Meis1a leukemia progression model for their potential role as oncogenic and tumor suppressor miRNAs.



Robert Sroka

Born in 1985 in Leipzig, I studied Biology at the Johann Wolfgang Goethe University, Frankfurt am Main. Since 2013, I have been a member of the PhD Programme in Molecular Medicine at the International Graduate School of Ulm University. I am performing research for my PhD thesis in the lab of Professor Seufferlein at Ulm University Hospital (Internal Medicine I).

Michael Stalmach

Born in Ulm in 1994, I have been studying Medicine at Ulm University since 2012. I became a member of the working group in the Molecular Biology Research Laboratory and focused on Oncology under the direction of Dr. Claudia Friesen at the Institute of Forensic Medicine. I have been taking part in the doctoral study program in Experimental Medicine (Promotionsprogramm Experimentelle Medizin) at the IGradU since 2015.

Role of Protein Kinase D1 (PKD1) in the control of adherens- and tight-junction integrity.

Epithelial cells are tightly interconnected and form two-dimensional multicellular sheets. Cell-cell adhesion is mediated by specialized structures: adherens junctions (AJs) and tight junctions (TJs). AJs and, in particular, TJs establish barriers across epithelial sheets and mediate epithelial permeability. AJs are formed by transmembrane cadherins which recruit catenins and cytoskeletal adaptor proteins. Upon homophilic interaction of its extracellular domains, the intracellular domain of E-Cadherin associates with cytoplasmic proteins that provide a link of adhesion complexes to the actin cytoskeleton and dynamically regulate adhesion strength. Recent data suggest that the stable binding of adhesion complexes to F-actin requires mechanical force. Thus, together with the classical catenins, additional actin-binding and putative scaffolding proteins may control assembly and actin linkage of adhesion complexes. One example is the actin-regulatory protein, cortactin, which is an important part of the adhesion complex and directly binds to E-Cadherin. Cortactin is required for the cadherin–actin cooperation and actin accumulation that supports the formation of AJs. Our own data show that cortactin is phosphorylated at S298 by the serine/threonine kinase Protein kinase D1 (PKD1). In my thesis work, I am further elucidating the role of cortactin and its posttranslational modification by PKD1 in the molecular control of adhesion complex assembly during AJ formation and cell-cell adhesion.

Development of new therapy strategies for colon cancer by using opioids, especially D, L-Methadone

Colon cancer is one of the most common cancers in western industrial nations and is a malignancy of the large intestine with an incidence rate of 30-35 per 100,000 population. The survival rate of five years after onset of the disease may depend on the stage at 95% or 5%. The research group of Dr. Friesen has examined the impact of D, L-Methadone, a μ-opioid receptor agonist, in combination with chemotherapeutic agents and was able to show that the effect of chemotherapeutic agents may be enhanced by methadone addition. In this work, it will be examined whether D, L-Methadone allows a reduction in the dose of chemotherapeutic agents with fewer side-effects. The molecular mechanism of action is to be characterized to elucidate the enhancement of opioids. The project is focused on the molecular mechanisms of apoptosis induction. The mitochondrial (intrinsic) and the ligand-receptor (extrinsic) signal transduction pathways of apoptosis will be examined. Furthermore, the influence of the opioid receptor signaling pathway and, inter alia, the downregulation of cAMP are examined in the enhancement and induction of apoptosis. D, L-Methadone will be, inter alia, combined with the chemotherapeutics, irinotecan and 5-FU, which are also conventionally used for colon carcinoma. A commonly used method is the western blot analysis with antibodies against the main actors of apoptosis, e.g. initiator caspases 8 and 9. Quantification of apoptosis was measured by flow cytometry as described by Nicoletti.

Cora Stegmann

Born in Munich in 1987, I started studying Biology at Ulm University in 2007. Since 2012, I have been working at the Institute of Virology under the supervision of Prof. Christian Sinzger. In 2013, I started to work on my PhD project and became a member of the International Graduate School.

Daniela Steinbrecher

I studied Biology at Ulm University. Currently, I am undertaking my PhD studies at the Department of Internal Medicine III within the PhD Programme in Molecular Medicine of the International Graduate School.

Functional mapping of the human cytomegalovirus envelope glycoprotein O by mutational screening

The human cytomegalovirus (HCMV) is the most common infectious cause of sensorineural hearing loss. In contrast to other herpes viruses, the essential proteins, gB, gH and gL, are not sufficient for HCMV entry. Infectivity can only be accomplished by binding of gO to gH/gL. However, the exact role of gO remains inexplicit and, to date, it is an open question whether gO is mainly a chaperone for gH/gL or whether it directly binds cellular receptors. The aim of this study is to define important peptide sites within gO and, by this means, to explore the functions of the protein. gO is highly polymorphic and, therefore, the degree of conservation of a certain site can give a hint towards its function. Parts that are conserved among CMVs infecting different species most likely contribute to the most basic function of gO and the formation of the gH/gL/gO complex, whereas human CMV-specific sites of the protein are more likely to promote host-specific functions. Accumulations of charged amino acids are especially interesting due to their hydrophilicity and potential involvement in protein-protein interactions. Highly conserved peptide sites, as well as HCMV-specific charged clusters, are analyzed by seamless mutation of the respective amino acids and subsequent measurement of viral fitness. This mutational mapping will help to understand the role of gO. In the case of identifying potential receptor-binding sites, this knowledge can eventually be translated into novel CMV therapies.

Mechanisms that confer resistance to the small molecule inhibitor ABT-199 in chronic lymphocytic leukemia

Chronic lymphocytic leukemia (CLL) is the most common adult leukemia in the Western world. It is characterized by the accumulation of CD5+ mature B-lymphocytes with high levels of the anti-apoptotic protein B-cell lymphoma 2 (BCL-2) in the blood, bone marrow and lymphoid organs. Immunochemotherapy is still considered the standard first-line treatment for CLL. However, in recent years, small molecule inhibitors such as ABT-199 have been shown to be highly efficacious. ABT-199 selectively binds and inhibits BCL-2 by mimicking the BH3 domain and displacing the sequestered pro-apoptotic proteins, thus inducing apoptosis and therefore providing a highly specific and efficacious treatment approach to this disease. ABT-199 as a monotherapy has already been shown to be highly effective in high-risk CLL independent of genetic alterations. However, resistance to ABT-199 has occurred during treatment and little is known about the mechanisms and genes that are involved. Therefore, the aim of my thesis is to identify genes that are involved in mediating resistance to ABT-199.

Fabian Stiefel

Born in 1984, he studied Chemistry at the University of Freiburg and Biotechnology in a trinational program at the Ecole Supérieure de Biotechnologie de Strasbourg (ESBS). In 2012, he started his PhD at the Biberach University of Applied Sciences and Ulm University in the Cooperative PhD Program (Kooperatives Promotionskolleg - KPK).

Katja Stifter

Born in 1987, I completed my diploma in Biology, with my focus on Molecular Biology, at Ulm University. Since the time of my diploma thesis, I have been working in the group of Prof. Dr. Reinhold Schirmbeck in the Department of Internal Medicine I at Ulm University Hospital. For my PhD studies, I am also a member of the DFG-funded research training group, CEMMA.

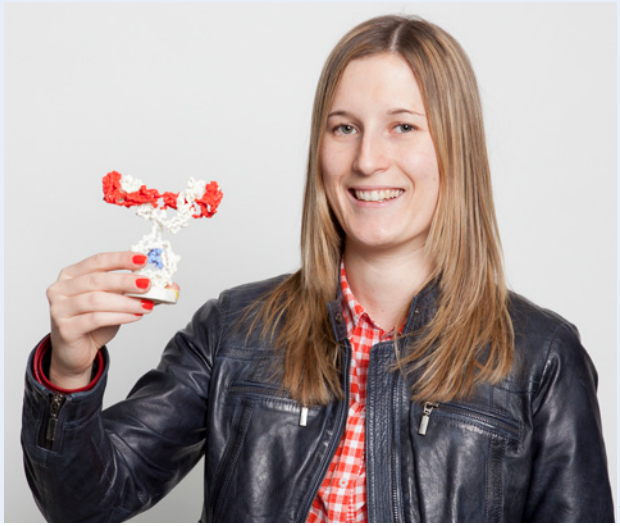
Profiling process relevant microRNAs in CHO cell lines during biphasic bioreactor cultivations.

The complex nature of biopharmaceutical proteins such as antibodies leads to their mandatory production in mammalian cell lines to achieve the necessary requirements for biological activity, correct protein folding and preventing adverse immune reactions in humans. The most common mammalian host for industrial-scale production is the Chinese hamster ovary cell line. Mammalian cell culture in bioreactors faces many challenges, such as, limited growth capacities, low viable cell concentrations and productivity. Optimization strategies focus mainly on bioprocess advancements and classical cell line engineering methods to overexpress single genes which increase the burden of the translational capacity of cells.

In contrast, microRNA (miRNAs) have interesting properties for cell-line engineering. MiRNAs are small non-coding RNAs that function as fine-tuning regulators of posttranscriptional gene expression and are involved in crucial regulations of many signaling and metabolic pathways. MiRNAs can target many dozens of mRNAs and thus have a high impact on the regulation of gene expression without overcharging the translational machinery of the cell. The aim of our studies is to establish miRNA profiles for different CHO cell lines, cell culture phases and bioprocess conditions and evaluate their influence on process relevant parameters such as proliferation, viability and specific productivity. This increased knowledge of miRNA regulation in CHO cells may pave the way for introducing a new layer of control for pharmaceutical cell-line engineering.

Induction and prevention of autoreactive, preproinsulin-specific CD8 T cell responses in young and old mice by DNA- and protein-based immunization

Diabetes mellitus type I (T1D) is hallmarked by a breakdown of central as well as peripheral tolerance mechanisms and the concomitant activation of autoreactive CD8 and CD4 T cells targeting and destroying pancreatic β-cells. Due to rare treatment possibilities, the establishing of prophylactic vaccine strategies to inhibit induction of autoreactive CD8 T cells and T1D would be beneficial. Our work group has established mouse models to study the *de novo* induction of preproinsulin (ppins)-specific CD8 T cells and experimental autoimmune diabetes (EAD) by DNA-based immunization. A single injection of ppins-encoding plasmid DNA efficiently induces EAD, e.g. in PD-L1-KO mice. In my PhD project, I use these murine models to address several points. First, I try to define antigens and antigen formulations that specifically induce or inhibit ppins-specific CD8 T cells and EAD in young mice. Second, we are interested in the role and function of $CD4^+$ $Foxp3^+$ regulatory T cells in the protective immune responses, as these cells serve as a promising target in the context of future immunotherapies against autoimmune syndromes. Lastly, we want to characterize differences in autoreactive and protective immune responses in young and old mice. This is important to the extent that age-associated immune deficiency, brought about by natural age advancement (“immune senescence”), manifests, inter alia, as increased onset and progression of autoimmune diseases.



priv.

Martina Stützle

Born in 1985, she studied Pharmaceutical Biotechnology at the Biberach University of Applied Sciences and Ulm University. She has been a PhD student at the Institute of Pharmaceutical Biotechnology since 2012. Her research is part of a joint PhD program in Pharmaceutical Biotechnology established by Ulm University and the Biberach University of Applied Sciences and is funded by the Ministry of Science, Research and Arts of the state of Baden-Württemberg.

Development of protein aerosols for intranasal nose-to-brain drug (N2B) delivery

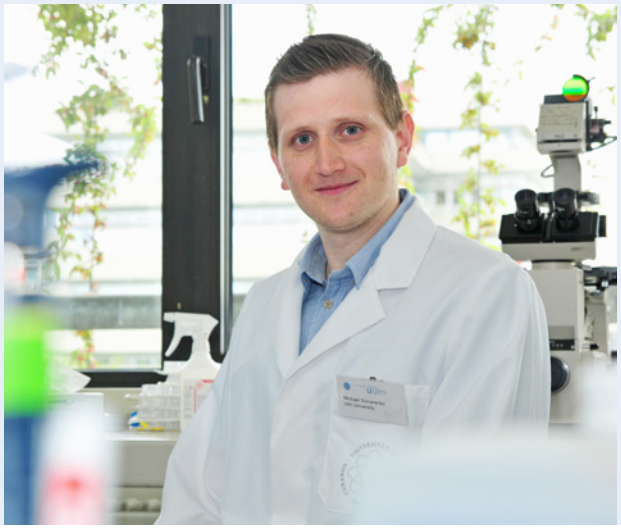
Therapeutical antibodies for the treatment of central nervous system diseases are the focus of this PhD project. By intranasal application of pharmaceutically active components, the natural barrier to the brain, that is, the blood-brain barrier, can be bypassed. Previously, it has been shown that peptides and small proteins are able to be transported from the olfactory epithelium to the olfactory nerve and from there to other brain areas. An antibody and its fragments were biotechnologically generated and purified using different expression systems and chromatographic steps. The constructs were formulated for improved protein stability to ensure identity, activity and purity during aerosol generation. Suitable dispersion systems were evaluated for aerosolization in respect to particle size, flow rates, chemical and physical properties, as well as material and time. Moreover, a standardized human nose averaged out of 30 CT-Scans was used for simulation deposition studies at the olfactory epithelium. In order to validate the numerical computational fluid and particle dynamics model, the aerosol flow velocity and deposition results were compared with an experiment using a constructed rapid-prototyped model. Finally, a nasal epithelial cell model was developed to study the drug transport of deposited antibody aerosol in an air-liquid interface cloud system. The acquired knowledge will be regarded as a validated platform that is transferrable to any other antibody fragment with a certain size for N2B drug delivery.

Narmadha Subramanian

Born in 1989, I started at the Institute of Virology in 2013 after entering Ulm University in 2011 to complete my master's in Biomaterials. While completing my Master thesis in Electron Microscopy and Virology, I gained an interest in the field of Virology. My admission to the PhD program at the International Graduate School of Molecular Medicine, under the supervision of Prof. Dr. Thomas Mertens, has provided me with an immense scope to continue my research in Virology.

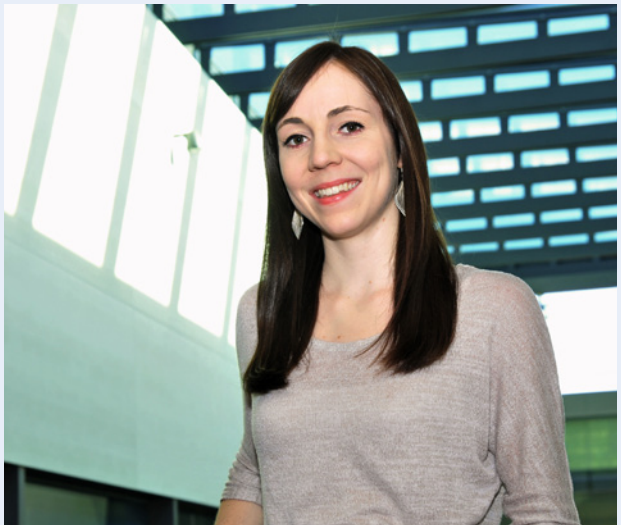
Role of naïve T cells in HCMV transmission

Human cytomegalovirus, being present in 60-70% of the human population, causes mortality and morbidity in immunocompromised patients. Although there are various techniques to titrate the virus, there are still very few methods to quantitate the virus transmission in cells. Initially, we established a technique to determine the transmission Kinetic and then phenotypically characterize the HCMV strains based on the mode of transmission of the virus in cells *in vitro*. Then, as an application, immune cells were applied to the same method to determine the inhibition provided by different immune cells. Seronegative T Cells control over the transmission surprised us due to the absence of both antigen-specific and memory T cells. The second part of my project was to determine the role of seronegative naïve T cells in the transmission assay. The naïve T cells controlled the transmission to a certain extent even in an autologous condition and without any cytokine addition. The third part of my project is to prime the naïve T cells from a seronegative donor to determine its role in HCMV transmission and to establish the phenomenon involved.



Michael Svinarenko

I was born in 1987 in Karabalta, Kyrgyz Republic. In 1996, my family and I moved to Germany. I completed my master's in Biomedical Engineering at the Albstadt-Sigmaringen University of Applied Sciences in 2014. In the same year, I started my PhD at the Department of Internal Medicine I and joined the International Graduate School in Molecular Medicine Ulm in the winter term of 2014/2015.



Tatjana Maria Swerev

I was born in 1992 and began to study Medicine in 2011. In February 2015, I started to work on my doctoral thesis at the Institute of Physiological Chemistry under the supervision of Prof. Dr. Wirth and Dr. Alexey Ushmorov. I participate in the study program in Experimental Medicine of the International Graduate School in Molecular Medicine Ulm and in the Mildred Scheel Doctoral Program (Mildred-Scheel-Doktorandenprogramm) offered by German Cancer Aid.

Analysis of the sequence of inflammation and p53 deletion in hepatocarcinogenesis

The risk of developing liver cancer is significantly increased by chronic HBV/HCV infection, excessive alcohol consumption, and aflatoxin B1 exposure. At the molecular level, human hepatocarcinogenesis is characterized by inflammatory responses, a loss of Trp53 function, telomere shortening and chromosomal instability.

Trp53 (transformation-related protein 53) is a tumor suppressor protein which plays a major and important role in the fate of a damaged cell by initiating cell repair, activation of apoptosis or senescence. In addition, Trp53 affects cellular differentiation and stem cell function. In human liver tumors, Trp53 mutations are associated with a poor prognosis.

The inflammatory microenvironment represents an essential component of every tumor. Chronic inflammatory responses in the liver are associated with the occurrence of liver fibrosis, cirrhosis and, also, hepatocellular carcinoma (HCC), in which more than 80% of all HCCs develop as a consequence of liver fibrosis or cirrhosis. In this context, NF-kB is an important transcriptional regulator that has an essential role in the regulation of inflammation in the liver.

In this project, two important characteristics of hepatocarcinogenesis will be addressed, namely, the modulation of an inflammatory milieu and the loss of the Trp53 gene function. This is intended for a better understanding of hepatocarcinogenesis and may lead to the identification of new targets which might be used for novel therapeutic approaches.

Potentiation of classical Hodgkin lymphoma sensitivity to epigenetic therapy

Patients suffering from classical Hodgkin lymphoma (cHL) generally have a good prognosis with conventional chemo- and radiotherapy. However, survivors often suffer from infertility, cardiotoxicity and from secondary malignancies. Therefore, searching for specific less toxic therapeutic modalities is warranted. Epigenetic therapy represents a specific and less harmful approach to cancer treatment. Epigenetic factors, including DNA methylation, contribute to the oncogenic program of cHL, for example, by the silencing of tumor suppressor genes. In fact, there has been an anecdotic case in which it was reported that the demethylating agent, decitabine, induces partial regression of relapsed cHL. In pilot experiments, our group discovered that decitabine strongly inhibits proliferation of cHL cell lines. With the help of gene-expression profiling (GEP), followed by gene set enrichment analysis (GSEA), we could show that decitabine induces not only silenced tumor suppressor genes, but also genes of main oncogenic pathways in cHL (JAK-STAT and NF-κB), including genes responsible for protection from apoptosis. We hypothesize that pharmacological inhibition of JAK-STAT, NF-κB, and related pathways might improve efficacy of decitabine. Therefore the aims of my project are to validate the GEP data and to investigate the influence of inhibition of the upregulated pathways on the antitumor effect of Decitabine using *in vitro* models. I hope that this study will help to optimize therapy of cHL.

Helen Tauc

I attained my B.Sc. with honors at the University of Oregon, USA. I then received a DAAD scholarship to travel to Germany and complete the M.Sc. program in Molecular Medicine at the Ulm University. After the M.Sc., I joined the IGradU and am currently in my fourth year as a PhD student at the Inst. of Biochemistry and Molecular Biology under the supervision of PD Dr. Petra Pandur.

Melanie Tepper

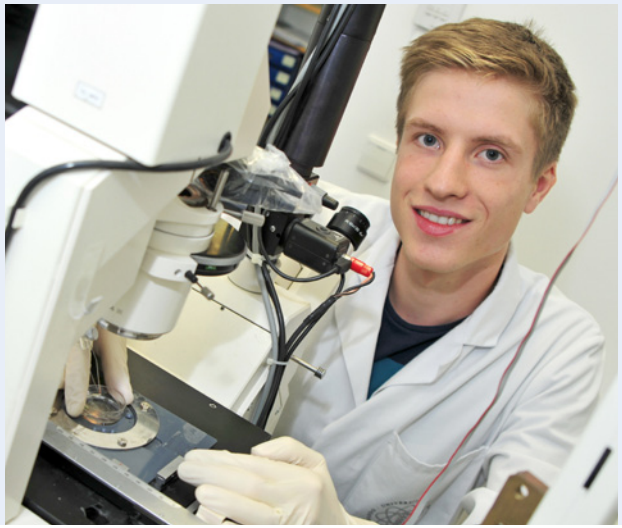
Born in 1988 in Saarbrücken, Germany, she is currently in the second year of her PhD studies in Molecular Medicine at the Institute of Physiological Chemistry under the supervision of Prof. Dr. Thomas Wirth. Besides her passion for science, Melanie loves traveling, discovering new cultures and lives according to the motto, "Learn from yesterday, live for today, hope for tomorrow. The important thing is not to stop questioning." (Albert Einstein)

Identifying Key Regulators of Aging in *Drosophila* Intestinal Stem Cells

The goal of the project is to uncover and characterize factors that contribute to stem cell aging in the adult *Drosophila melanogaster* (fruit fly) intestine, specifically the intestinal stem cells (ISCs) of the midgut. The integrity of the midgut critically depends on the proper function of ISCs, which maintain the gut epithelium. During aging, intestinal tissue homeostasis progressively deteriorates and the stem cells fail to regenerate the tissue to its normal state. The underlying causes of age-related changes in the molecular pathways controlling ISC behavior are still ambiguous. We wanted to identify molecules that are important in maintaining ISC integrity and function throughout aging. Having performed next generation RNA-sequencing on an enriched ISC population from young and old midguts, we identified many highly differentially expressed genes. These genes are attractive candidates to be studied further with respect to their function in aging. Currently, we are focusing on a gene encoding a chromatin remodeling factor that we show is crucial for maintaining the ISC population over time. Loss of this factor not only leads to a loss of stem and progenitor cells over time, but it also inhibits the normal proliferative response to tissue damage and stress in young flies. Currently, further analysis into the function of this gene is being carried out with the aim of gaining novel insights into the molecular mechanisms that drive aging.

Consequences of cell-type specific NF-κB modulation on the outcome of traumatic brain injury

Traumatic brain injury (TBI) represents a leading cause of morbidity and mortality, especially among young individuals below the age of 45 years. Subsequent to the primary impact, secondary TBI pathology develops over minutes to weeks after the actual incident and causes different metabolic, biochemical, molecular and cellular events, which contribute to additional tissue damage. Although TBI is a very complex process that, depending on the cause and severity, may involve distinct pathomechanisms, a rather common aspect is the posttraumatic development of a neuroinflammatory response. The NF-κB signaling pathway represents the main inflammation-mediating signaling pathway in mammalian cells and is activated in different cell types, including neurons, glial cells and endothelial cells. However, it is currently unclear whether NF-κB might have distinct functions, either detrimental or beneficial, in these different cell types. The aim of Melanie's thesis is to characterize the neuron- and oligodendrocyte-specific contribution of this critical signal transduction pathway to the outcome of head injury and to identify critical time points that could be selectively targeted during secondary TBI pathology.



Martin Textor

I was born in Munich in 1991 and am in the ninth semester of my studies in Medicine at Ulm University. I have recently started my doctoral dissertation under the supervision of PD Dr. Werner Melzer at the Institute of Applied Physiology. For my project, I received a scholarship from the International Graduate School of Molecular Medicine Ulm.

Umesh Tharehalli Mathada

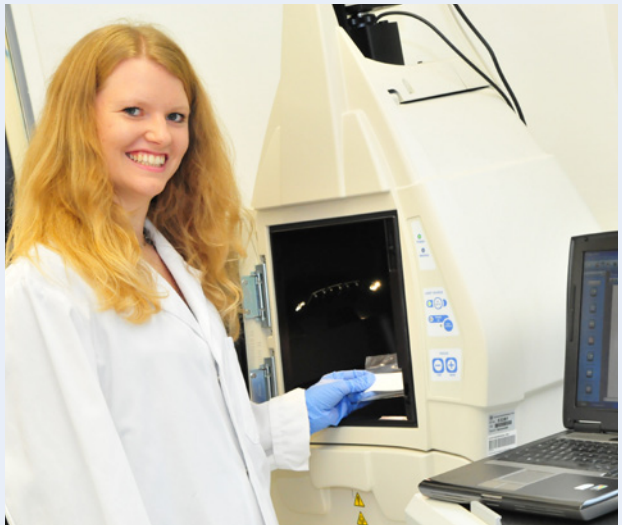
Born in 1990, I studied for my master's in Molecular Medicine at Ulm University from 2013 to 2015. Since the summer of 2015, I have been pursuing my PhD at the Institute of Internal Medicine I.

Studying skeletal muscle calcium release of a knock-in-mouse with the human malignant hyperthermia mutation Y522S in the ryanodine receptor

The research of my thesis is linked to malignant hyperthermia, a pathological condition that mainly originates from mutations in the gene which encodes the ryanodine receptor RyR1. This protein is a giant ion channel that releases calcium from the sarcoplasmatic reticulum in muscle cells in response to cell membrane depolarization and leads to contraction. In muscle cells with an MH mutation, RyR1 can be pathologically opened by different stimuli, for instance, by volatile anesthetics. The result is muscle rigidity and a hyper-metabolism in which the body temperature rapidly rises. Without treatment, the condition would be fatal. My project focuses on the unresolved question of how anesthetic- and voltage-induced activation of RyR1 affect each other. I will investigate if the normal action potential-induced gating of the RyR1 is different when the muscle cells are stimulated with the anesthetic agent, halothane. In addition, the modulating role of elevated temperature will be studied. For the experiments, I shall use a mouse model of MH (exhibiting human RyR1 mutation Y522S). The action potentials will be induced with extracellular electrodes and the membrane potential will be recorded by intracellular electrodes. The calcium release will be measured with a fluorescent indicator dye.

Modulation of hepatocellular carcinoma in a p53-deleted mouse model

Liver cancer is the sixth most common cancer in the world and associated with poor prognosis and is significant cause of mortality in developing and developed country. Based on cell type of origin and status of differentiation, primary liver cancer is classified as hepatocellular carcinoma (hepatocytic origin), cholangio carcinoma (cholangiocytic origin) and combined hepatocellular-cholangiocarcinoma (features of both hepatocytes and cholangiocytes). A previous study in the laboratory demonstrated that p53 deletion in the liver was a single event in the induction of liver tumors with liver tumors majority being mixed differentiated tumors. The aim of this project is to analyze the influence of p53, one of the most frequent mutated tumor suppressor genes in liver cancer, and Notch during hepatocarcinogenesis. Therefore, we are analyzing the effect of activation and inactivation of Notch signaling in liver tumor cells with loss of p53 on proliferation, differentiation, and tumorigenic potential. For this approach we are using the mouse and human liver cancer cell lines with different p53 status (wild-type or deleted/mutated) in which we activate Notch signaling by overexpression of Notch cDNA or inactivate Notch signaling by shRNA mediated knockdown of Rbpj. These cells will be analyzed for proliferation, invasion, migration, and differentiation. The tumorigenic potential we will determine in vivo in the CAM assay as well as after transplantation in immunodeficient mice. The tumors will be monitored for size as well as progression and differentiation status.



Daniela Christine Tradowsky

Born in 1988, I obtained my bachelor's and master's degrees from the University of Bonn and Ulm University, respectively. Since 2015, I have been a PhD student at the IGradU and work at the University Hospital Ulm, Clinic for Psychosomatic Medicine and Psychotherapy, in the group for Clinical-Experimental Stress Research, under the supervision of PD Dr. Christiane Waller.

Bernadette Maria Trojanowski

Born in 1984 in Peiskretscham, Poland. Since 2013, she has been working at the Institute of Physiological Chemistry where she is analyzing the role of NF-κB deregulation in pancreatic β-cells and its influence on diabetes development as well as the regulation of β-cell maintenance and of possible regeneration processes.

Expression and signaling of the oxytocin receptor system in peripheral organs

Oxytocin is mainly known as an important hormone involved in uterus contraction during labor, lactation and bonding. However, oxytocin also plays a major role in the peripheral organ system, for example, in the cardiovascular system, where oxytocin causes vasodilatation, decreased heart rate, and a reduced contractility, and in the gastrointestinal tract where oxytocin regulates motility and inflammation. Furthermore, oxytocin is involved in stress responses and is known as an anxiolytic hormone. So far, no studies have been conducted to evaluate the involvement of the oxytocin system in stress reactions in the cardiovascular and gastrointestinal system.
Thus, the aim of my PhD thesis is to examine how the oxytocin system is modulated by stress reactions in peripheral organs. We use different mouse models of social and attachment stress that are analyzed for oxytocin receptor signaling, oxytocin plasma concentrations as well as morphological and functional changes. Further studies will focus on the translation of our animal study results into humans. Therefore, we will perform studies with patients suffering from stress-related diseases.

Mechanisms of IKK/NF-κB-dependent diabetes development

Our general understanding of type 1 diabetes (T1D) pathogenesis has profited greatly from two spontaneous animal models, namely, the non-obese diabetic (NOD) female mouse and the biobreeeding rat (BB) which both phenocopy several aspects of the human disease. However, the translational prediction of therapeutic interventions in man based on findings in these animal models noticeably failed. Therefore, there is still a need for novel animal models mimicking critical aspects of human T1D pathology.
The pathogenesis of human T1D is characterized by a progressive destruction of insulin-producing β-cells during the course of inflammatory reactions. As a key regulator of inflammation and cell survival, activation of the IKK/NF-κB signal transduction system can critically influence the course of the disease. In order to investigate the role of the IKK/NF-κB signal transduction system in β-cell homeostasis, two complementary mouse models (gain- and loss-of-function) were generated at our institute. In both models, the animals spontaneously develop full-blown diabetes with insulitis, hyperglycemia and hypoinsulinemia. Microarray-based gene-expression profiling revealed novel and so far uncharacterized genes in the context of diabetes. Furthermore, both animal models are able to recover from the diabetic phenotype after switching off transgene expression. Therefore, the main objective is to identify the molecular mechanisms by which β-cell functionality can be restored.

Timo Trzaska

Born in 1990, he started his medical studies at Ulm University in 2010. To gain insight into the world of research, he decided to write his doctoral thesis on fundamental research and joined the study program in Experimental Medicine in 2014. He performs his experiments in the Department of Transfusion Medicine.

Verena Vieres

She was born in 1991 and is now studying Medicine in the 8th semester at Ulm University. She is currently working on her doctoral thesis at the Institute of Orthopedic Research and Biomechanics in the Spine Group, which is led by Prof. Dr. Hans-Joachim Wilke, and receives support to participate in the study program in Experimental Medicine.

The effect of granzyme B in antigen-presenting cells

The serine protease granzyme B is most commonly known from cells such as cytotoxic T cells (CTL). Here it mediates apoptosis in target cells together with perforin. However, over the last few years, many non-cytotoxic functions of granzyme B, such as regulatory functions and cleavage of ECM proteins, cell-surface proteins and autoantigens, have been described. Importantly, it has been shown that this enzyme can play a major role in antigen-processing of antigen-presenting cells (APC).

In my project, I am taking a closer look at these functions. I want to shed light on the importance of granzyme B in the processing and uptake of antigens as well as in the resulting modulation of antigen-specific T cells. Therefore, I examined conditions that stimulated B cells and plasmacytoid dendritic cells (pDC) to produce granzyme B. I then prepared lysates of tumor cells which were given to these APC to examine the effect of granzyme B on the uptake of tumor antigens. Next, these cells were used in a co-culture to generate antigen-specific T cells.

Ultimately, the goal of my project is to show that a temporary induction of granzyme B in B cells and pDC enhances their function as antigen-presenting cells and that, depending on the dynamics of the granzyme B induction, these cells can exercise regulatory or immunostimulatory functions.

The structure and anatomy of the cervical disc and the correlation of whiplash trauma and degenerated discs

The structure of the cervical disc is up till now not known in detail. It is often considered as a smaller lumbar disc. The different kinematics of the cervical spine suggest that the structure must be different and this has already been shown macroscopically by Mercer et al in the case of C6/7.

The goal of this thesis is to provide accurate data of the structure for each of the five discs to generate a finite element model of the cervical spine.

Verena Vieres is using 23 human cervical spines, of which 21 were tested in a whiplash simulator in an earlier study. Therefore, her second aim is to look for a correlation of degenerated discs and the pattern of injury during whiplash. In order to describe the three-dimensional structure of the cervical disc, for each of the five cervical discs, three proper specimens were selected from the 21 whiplash specimens. Those 15 discs will be further examined in defined cuts to measure the geometrical data of the annulus and nucleus in multiple planes.

Additionally, two untested specimens will be examined very closely in 500µm steps to replace the MRI scan, which cannot provide data as exactly as required.

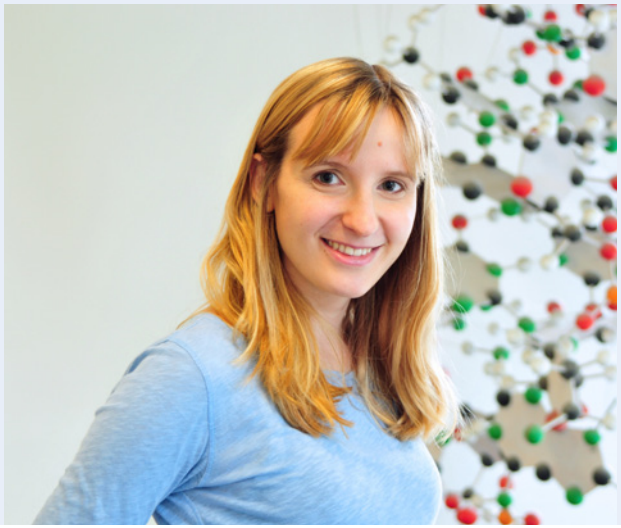
This data will then be used in another study of the institute to develop a finite element model of the cervical spine.

Additionally, X-Rays of the spines were classified into degrees of degeneration.

The degree of degeneration will be compared to the range of motion measured by a spinal loading simulator and the macroscopically visible damages to find a correlation.

Timo-Daniel Voss

He was born in 1991. After his bachelor's studies in Biology, which focused on Human Physiology, at the University of Hohenheim (Stuttgart), he went to Ulm University and focused on Neurobiology in the master's program in Biology. In October 2015, he started his PhD project at the IGradU in the Department of Neurology under the supervision of PD Dr. med Jan Lewerenz.



Sophia Vuckovic

Born in 1992, I am currently in the ninth semester of my medical studies at Ulm University and am pleased to have been accepted into the doctoral program of study in Experimental Medicine. Since I am intrigued by the workings of the nervous system, I decided to do my doctorate in the Arnim work group at the Institute of Neurology and to focus my research on Alzheimer's disease.

Generation of a doxycycline-dependent astrocyte-specific EAAT2-transgenic mouse to investigate neurodegenerative disease

The excitatory amino acid transporter 2 (EAAT2) is mainly expressed in astrocytes and mediates the reuptake of excitatory neurotransmitter glutamate (glu). Many neurodegenerative or neuroinflammatory diseases, including amyotrophic lateral sclerosis (ALS), multiple sclerosis, Alzheimer's and Huntington's disease, show downregulation of EAAT2 that possibly leads to a glu dysbalance and subsequent excitotoxicity. However, the pathophysiological importance of chronic excitotoxicity in neurodegenerative and neuroinflammatory disease has not been unequivocally demonstrated.

To generate preliminary data, a VSV-G-tagged murine EAAT2 was sub-cloned into the pBI-5 vector that allows doxycycline-dependent gene expression. Upon transient over-expression of the construct in A172 glioblastoma cells along with co-expression of a Tet transactivator, a doxycycline-inhibitable EAAT2 activity could be demonstrated using ^{3}H-glutamate uptake assays.

This construct will serve as a starting point for the generation of a transgenic mouse model that allows a doxycycline-dependent over-expression of EAAT2 in astrocytes. This mouse will be characterized within the PhD project. By combining it with animal models of neurodegenerative diseases, this mouse model will allow the testing of the hypothesis of glu dysregulation in neurodegeneration and neuroinflammation.

Analysis of the impact of the potential Alzheimer-relevant GULP1 protein on the morphology of primary hippocampal neurons

Today, we know that both the precursor protein, APP, and the tau protein play key roles in the pathogenesis of Alzheimer's disease. APP is proteolytically cleaved into beta-amyloid, the main component of amyloid plaques found in the brains of patients with Alzheimer's disease. Hyperphosphorylated tau protein aggregates to form neurofibrillary tangles, which is also a histopathological hallmark of Alzheimer's disease.

Although APP and tau have been identified as key proteins in Alzheimer's disease, their connection remains unclear. However, current studies in our laboratory work group have already given preliminary insight into this matter by having succeeded in showing that the engulfment adaptor PTB domain containing 1 (GULP1) binds both APP as well as tau and thus links the two key proteins of Alzheimer's disease. In my doctoral thesis, I now analyze mainly whether the recently shown interaction of GULP1 with tau and APP induces morphological effects on hippocampal neurons. For this purpose, I produce GULP1 and control lentiviruses, and then use these to transduce primary hippocampal neurons. After immunostaining, it is then possible to examine with a fluorescence microscope the assumed morphological distinction between the GULP1 overexpressing neurons and the control neurons. With the results of this project, I hope to contribute to a better understanding of Alzheimer's disease on a molecular basis.

Karolin Walter

Born in 1990, I started studying as a PhD student in the Department of Internal Medicine I at the University Hospital in the summer semester of 2015 after having already finished my bachelor's and master's in Biology here in Ulm.

The role of the enzyme telomerase and the telomere length in pancreatic cancer stem cells

Cancer stem cells are a subpopulation of exclusively tumorigenic and highly therapy-resistant cancer cells that share certain features with stem cells, such as unlimited self-renewal and gene-expression patterns, and the ability to give rise to (heterogeneous) progeny by symmetric and asymmetric division. For normal stem cells, a correlation between telomerase activity, telomere length, longevity and thus a virtually unlimited proliferation potential has previously been shown.
By rigorous testing *in vitro* (gene and protein expression, colony formation) and *in vivo* (tumorigenicity, cancer stem cell frequency, metastatic activity), we will investigate the relevance of telomerase activity and subsequent telomere length in pancreatic cancer stem cells isolated from patient primary pancreatic cancer samples. Furthermore, we will test new drugs by specifically targeting telomerase to evaluate their effects on the cancer stem cell population, tumor composition, and survival. Altogether, these investigations will enhance our understanding of this highly dangerous cell population and will hopefully enable us to develop new and targeted therapies against pancreatic cancer.

Fan Wang

I am conducting research at the Institute of Physiological Chemistry and my current project is to investigate the role of FOXO1 in the oncogenic program of acute lymphoblastic leukemia. This research will help to clarify the role of FOXO1 in the oncogenic program of B-ALL and will provide a rationale for B-ALL treatment by targeting FOXO1.

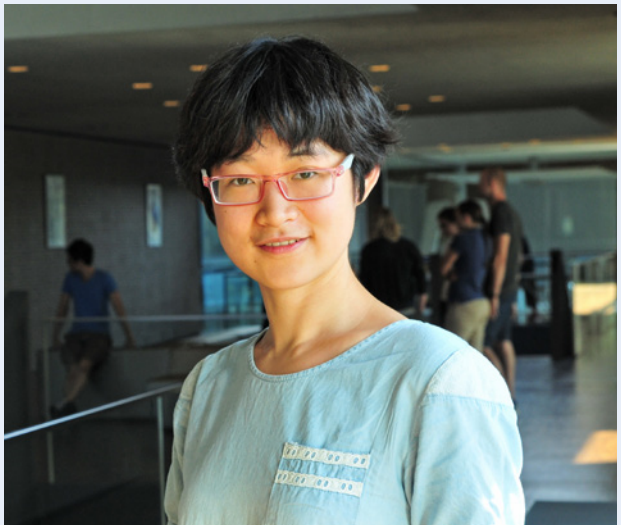
The role of FOXO1 in the oncogenic program of acute lymphoblastic leukemia

Treatment of pre-B-cell acute lymphoblastic leukemia (B-ALL) in children has shown an eminent progress over the past decades. Nevertheless, about 15% of patients cannot be cured. The life-threatening complications of conventional chemotherapy dictate the search for new therapeutic targets.
FOXO1, together with other transcription factors that include EBF1, PAX5 and TCF3, plays a central role in the differentiation of pre-B-cells. In cooperation with PAX5, FOXO1 induces the expression of Syk, Blnk, Rag1, Rag2, Aicda and IL7RA genes. Of note, SYK and IL7RA signaling contributes to the oncogenic program of B-ALL which utilizes the pre-B cell survival and proliferation program. Moreover, FOXO1 level is preferably expressed in B cells and at very high levels in the early stages of B cell differentiation (Gene Enrichment Profiler).
Previously, by comparing human B cell lymphoma cell lines, we found the highest levels of FOXO1 expression in the B-ALL cell line, Reh. In subsequent experiments, we found high FOXO1 expression levels in most of the B-ALL cell lines. We also found that pharmacological inhibition of FOXO1 specifically induces cell death of B-ALL, but not other B- and T-lymphoma cell lines. Furthermore, we found that pharmacological inhibition of FOXO1 shows a strong antitumor effect against B-ALL explantates *ex vivo* and *in vivo*. We conclude that FOXO1 is a critical component of B-ALL oncogenic program and its targeting represents a new approach for treatment of B-ALL.

priv.

Pei Wang

Born in 1985, she began her PhD studies in May 2013 at the Institute of Analytical and Bioanalytical Chemistry. Her research interest focuses on using infrared spectroscopy to identify available biomarkers for neurodegenerative disease diagnostics, as well as developing an effective method of discriminating the characteristics of disease-associated protein aggregation in relevant biosamples.



Shuang Wang

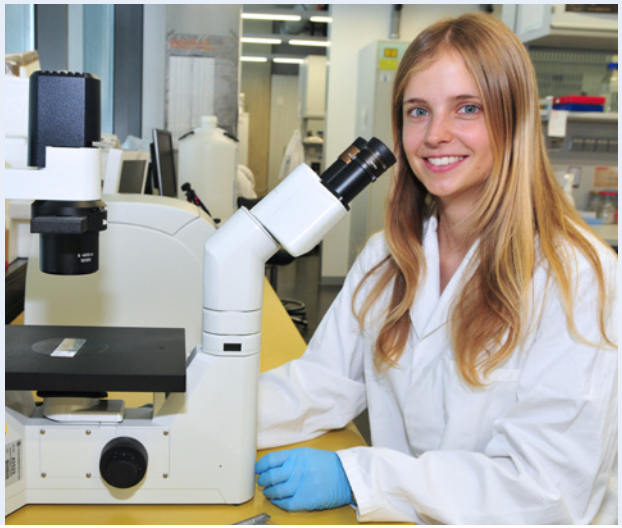
Born in 1987, I am studying at the Institute of Physiological Chemistry and am focusing my work on the pancreas, My current PhD thesis analyzes the role of NF-κB-inducing kinase (NIK) in pancreatic tumorigenesis and pancreatitis.

Infrared spectroscopy as a diagnostic tool for neurodegenerative diseases

Amyloid aggregation of a variety of proteins is associated with neurodegenerative diseases. A distinct feature of protein amyloid aggregation is the secondary structure change evident via increased crossed β-sheet conformations. Infrared attenuated total reflection (IR-ATR) spectroscopy is a sensitive optical technique that has the potential of providing secondary structure characteristics of proteins, via the analysis of the amide I band in label-free biological samples. This PhD project aims at using IR-ATR spectroscopy to analyze the characteristics of protein misfolding and aggregation in order to provide an available reference for early diagnostics of neurodegenerative diseases. To achieve this goal, an analytical model and ratiometric parameters were established to reveal the relationship between the IR spectra of protein mixtures, with and without amyloid fibrils, by using spectral curve fitting and simulation methods. Furthermore, natural polyphenols were applied as remodeling agents for disaggregating amyloid oligomers. Currently, IR-ATR sensor modification for protein immobilization is under investigation. Via this technique, a target protein and its conformations in physiological fluids will be specifically immobilized on the surface of an ATR sensor and their structure spectra would then be analyzed and compared between control and disease samples.

The role of NF-κB-inducing kinase (NIK) in pancreatic tumorigenesis and pancreatitis

Pancreatic carcinoma is the fourth leading cause of cancer death with a five-year survival rate of only 3-8%. The causes of pancreatic carcinoma are multifactorial. Repeated acute pancreatic injury and inflammation are considered crucial contributing factors to the development of pancreatic cancer. Studies in which the NF-κB signaling pathway is inhibited show a decline of tumorigenesis in pancreatic cancer cell lines. The less studied alternative NF-κB pathway relies on NF-κB-inducing kinase (NIK) as a direct upstream kinase for IKK^{α}. Once activated by NIK, IKK^{α} induces the processing of p100 to p52 which then together with RelB translocates to the nucleus. It is known that NIK is involved in pancreatic cell-line proliferation. Recent research also claims NIK upregulation combined with decreased expression of NIK inhibitor TRAF2 was observed in human PDAC samples. Thus, the characterization of the role of NIK in pancreatitis and pancreatic carcinoma could direct the development of appropriate therapies.

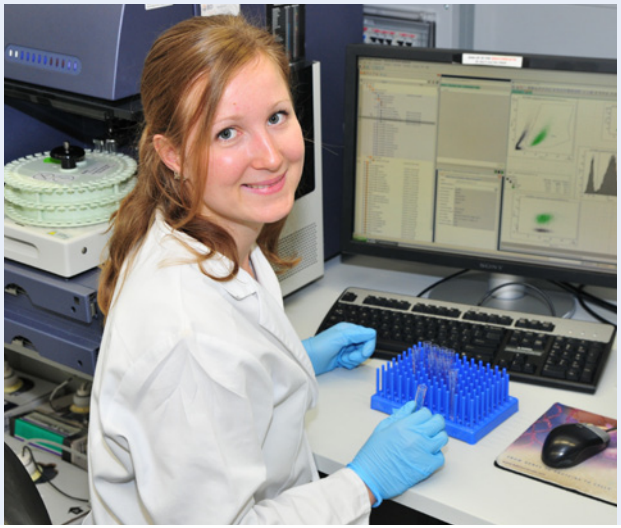


Renate Wanner

I was born in 1989 and completed my bachelor's and master's studies in Molecular Biology at Ulm University. To research my doctoral thesis, I remained at Ulm and work at the Institute of Physiological Chemistry (AG Knöll). I joined the PhD program of the Graduate School in October 2015.

The impact of traumatic brain injury on neuronal integrity and nerve regeneration: gene expression, mechanisms and neuroprotective strategies

This research focuses on traumatic brain injuries which are a frequent kind of injury, especially among younger people, and lead to brain dysfunctions, disabilities and death. In my project, I investigate the consequences of traumatic brain injury on axonal regeneration by targeting the facial nerve in mice. To quantify the regenerative process of the facial nerve, I perform functional and histological studies to analyze the whisker movement, motoneuron regeneration, neuromuscular synapse recovery and neuronal growth cone dynamics. I also want to analyze the molecular and cellular effects of facial nerve trauma. Consequently, I want to compare traumatic nerve injury to a complete surgical nerve transection, which has already been performed in my working group before. Moreover, I plan to study the role of SRF and ATF3 in facial nerve trauma since both transcription factors are hypothesized to have a beneficial role in nerve restoration.



Clarissa Dominique Weitzer

I was born in 1990 and started studying Molecular Medicine in 2009 at Ulm University. In 2014, I started my PhD at the Institute of Physiological Chemistry and am now working on the role of FOXO transcription factors in the pathogenesis of classical Hodgkin lymphoma and multiple myeloma.

Contribution of FOXO transcription factors to the pathogenesis of multiple myeloma

Multiple myeloma (MM) is one of the most frequently occurring hematological diseases in the world. It is characterized by a high clonal heterogeneity of malignant and terminally differentiated plasma cells that renders treatment of MM patients difficult. Although there have been several advances in therapy over the past years, MM is still incurable.
FOXO (forkhead box O) transcription factors regulate genes involved in oxidative stress resistance, cell cycle arrest, and tumor suppression. Also, they are important for B-cell development and differentiation. Recently, our group reported that FOXO1 acts as a tumor suppressor in classical Hodgkin lymphoma and that it directly activates the master regulator of plasma cell differentiation, PRDM1. In addition, we found that FOXO3 expression is high in MM. Therefore, we now investigate the role of FOXOs in MM using cell lines and clinical material. We hope that our findings will help to develop new approaches for the treatment of MM.

Jens-Uwe Werner

Born in 1989, I joined the International Graduate School in Molecular Medicine in Spring 2015 and am working on my Thesis in Prof. Dr. Knippschild's lab. His workgroup belongs to the Department of General and Visceral Surgery.

Miriam Werner

I was born in 1988 in Schwäbisch Hall and since 2011, I have been studying Medicine at Ulm. In the sixth semester, I decided to do my medical doctorate by engaging in experimental work in a laboratory. In February 2015, I therefore started my medical dissertation at the Institute of Virology by entering the study program in Experimental Medicine at the Graduate School in Molecular Medicine.

Role of severe obesity in the healing of muscle injuries

Adipose tissue functions are dysregulated in obesity and ultimately lead to changes in the release of growth factors, such as adipocytokines, cytokines, chemokines, hormones, and fatty acids, which are secreted from adipocytes and macrophages resident in white adipose tissue. These changes affect lipid metabolism, glucose homoeostasis, inflammation, angiogenesis, hemostasis and blood pressure. Co-morbidities, such as heart disease, diabetes, metabolic syndrome, hypertension, sleep apnea, and cancer, are also observed. Evidence shows that obesity impairs tissue regeneration processes after trauma. For example, obesity negatively affects regeneration of skeletal muscle injuries, although the underlying mechanisms have not yet been elucidated. Muscle regeneration can be divided into the initial and degenerative response, and the structural and functional recovery phase. It is a highly synchronized process demanding the timely coordinated activation of different cellular responses by various signaling molecules. Certain clues indicate the involvement of toxic lipid metabolites, pro-inflammatory adipocytokines and chemokines as well as leptin and insulin resistance that impair these processes (especially satellite activation and function) and finally result in decreased regenerative ability. The aim is to investigate: (i) the role of lipid metabolites and fatty acids on muscle regeneration; (ii) the consequences of an altered interplay between macrophages and stem cells; and (iii) how changes in signal transduction pathways affect satellite cell physiology.

The function of the glycans on the envelope protein pUL74 of human cytomegalovirus

Human cytomegalovirus (HCMV) relates to the family of betaherpesviridae. Some 50-99% of all people are seropositive for HCMV. The virus can cause massive disadvantages in unborn children in case of a primary infection of the mother. Also, HCMV infection or reactivation in patients under immunosuppression can result in severe disease. Despite huge efforts, it has not been possible to find an effective vaccination against HCMV up till now.
One explanation for the relative failure of antibodies to neutralize HCMV could be that the virus is somehow protected. For other viruses, such as HIV, it is already known that glycans on the envelope protein gp120 are able to shield the virus from the immune response. Such a protective function could also apply to glycoproteins in the envelope of HCMV. A promising candidate is the extensively glycosylated pUL74 (also known as gO) which forms a complex with gH and gL. Together, they play a key role in the entry into host cells. Despite the high polymorphism of gO among different strains of HCMV, the extent of glycosylation is conserved and indicates an important function of these glycans. The aim of my project is to test the hypothesis that some of the glycans on gO are important for immuneevasion. As removal of all glycosylation sites will probably hinder protein maturation, I try to generate an infectious virus with reduced glycosylation. With this mutated virus, I want to investigate whether glycans on gO prevent the induction of antibodies or hinder preexisting antibodies to neutralize the virus.

Rebecca Wiegner

Born in 1989, I began my bachelor's degree in Molecular Medicine at Ulm University in 2008 and continued in the master's program in 2011. I started my PhD thesis in the lab of Prof. Dr. Markus Huber-Lang in the Department of Orthopedic Trauma, Hand, Plastic and Reconstructive Surgery in 2013 and joined the PhD program of the International Graduate School in Molecular Medicine in 2014.

Rahel Stefanie Wiehe

I was born in 1986 and obtained my master's degree after studying Molecular Medicine at Ulm University. In 2014, I started my PhD thesis in the Department of Obstetrics and Gynecology in the laboratory of Prof. Dr. Lisa Wiesmüller.

A prospective study of the coagulation-complement crosstalk on leukocytes in polytrauma patients

Despite many attempts to improve treatment of patients before and after being hospitalized, severe trauma remains the leading cause of death in people below the age of 40. After trauma, a variety of danger-associated molecules is released that activate the complement and the coagulation system as one of the earliest molecular "warning systems." Excessive activation with fast consumption of cascade components, as seen in polytrauma patients, results in complementopathy and coagulopathy, and is associated with a poor outcome.

On a fluid-phase level, there is increasing evidence that complement and coagulation, previously believed to be two separate systems, interact intensively at various points, either by decreasing or augmenting cascade activation.

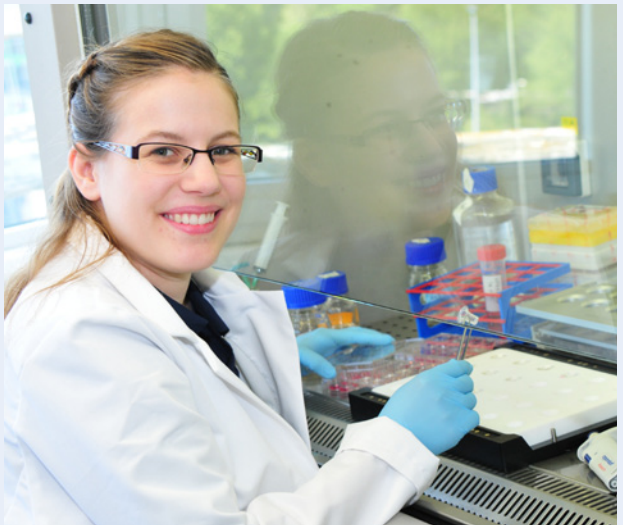
On a cellular level, endothelial cells interact closely with the coagulation system. Beyond that, however, there is some evidence that key molecules in coagulation are expressed on circulating immune cells. Therefore, I am working on the hypothesis that there is intensive crosstalk between complement and coagulation on the leukocyte surface, especially after polytrauma, and aim to identify the molecular mechanisms involved, by which leukocytes may contribute to posttraumatic coagulopathy and complementopathy.

Involvement of Endonuclease G in mitochondrial genome replication and transcription processes

Over the past years, great efforts have been made to solve the puzzle of mitochondrial (mt) DNA replication, but there are still many open questions and further research attempts are needed to fully understand in which way the mt genome is duplicated and which factors influence mt gene transcription. Endonuclease G (EndoG) is a nuclear-encoded endonuclease which preferentially cleaves guanosine-rich DNA regions. It was first assumed that EndoG is localized within the intermembrane space, but later on, it was shown to be bound to the mt inner membrane. The most well-known function of EndoG is the participation in nucleosome degradation during programmed cell death. Interestingly, EndoG is also capable of cleaving RNA and was suggested to generate RNA primers for the initiation of mtDNA replication. However, this hypothesis has not been pursued further since EndoG$^{-/-}$ mice did not show an effect in DNA copy number, structure or mutation rate. Indeed, EndoG regulates mt mass and function as well as Reactive Oxygen Species production in cardiac tissue. Also, involvement in regulation of gene expression of ND1, ND2, CoxII and ATPase6 could be shown. Despite the data situation, which is in part contradictory, I want to clarify in my PhD thesis whether EndoG plays a more important role in mt replication and transcription than previously expected.

Christoph Wille

Born in 1985, I studied Biology at the Johannes Gutenberg University of Mainz and started my PhD thesis in the laboratory of Prof. Dr. Seufferlein (Internal Medicine I) at Ulm University Hospital in 2012. Since 2013, I have been a member of the PhD program in Molecular Medicine at the International Graduate School of Ulm University.



Veronika Eva Winkelmann

Born in 1990 in Munich, she studied Molecular Medicine in Ulm. After completing her master's thesis at the Institute of General Physiology she became part of Prof. Frick's group and joined the International Graduate School in Molecular Medicine in April 2015.

Role of the Protein Kinase D family during constitutive secretion

Approximately half of the proteins generated by a cell have to be transported into or across at least one cellular membrane to reach their functional destinations. Therefore, protein transport is critical to maintain cellular homeostasis and dysregulation can contribute to diseases. A hallmark of pancreatic ductal adenocarcinomas is perineural and retroperitoneal invasion of tumor cells. Cancer cell invasion and eventually metastasis involve the degradation of the extracellular matrix and break-down of basal membranes by matrix-metalloproteinases (MMPs). The members of the Protein Kinase D (PKD) family, PKD1, -2, and -3 are involved in different signaling pathways and control, for example, cell motility, transcriptional activity and fission of vesicles from the trans-Golgi network (TGN), which is one of the major sorting hubs for lipids and proteins at the crossroads of the endocytic and exocytic pathways. Beside others, I was able to show for the first time that PKD1 and -2 control pancreatic cancer cell invasion and angiogenesis in an isoform-specific manner *in vitro* and *in vivo*. Additionally, I was able to show that PKD2 isoform specifically regulates constitutive secretion of the MMPs 7 and 9 in pancreatic cancer cells. In a follow-up project, I now try to clarify the underlying mechanism(s) of PKD2-controlled vesicle fission from the TGN. Additionally, I am also establishing a platform for high-throughput screening microscopy to measure secretion following knockdown of kinases by a full kinome shRNA library.

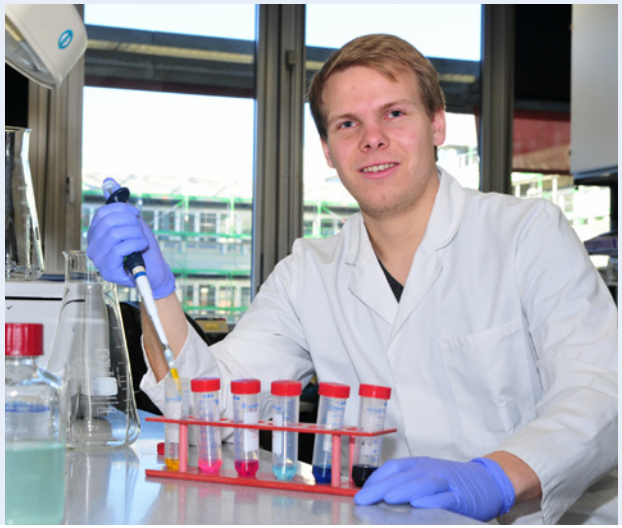
Cellular and molecular responses to trauma-induced damage of the distal respiratory epithelium

Alveoli are the central functional units of the lung where gas exchange between air and the blood takes place. Within the alveoli, two mechanisms are essential for maintaining alveolar homeostasis, namely, regulated fluid transport and secretion of pulmonary surfactant, which both require an intact alveolar barrier.

Trauma, whether of direct or indirect pulmonary origin, often results in structural and/or functional damage of this barrier. Damage to the alveolar barrier is therefore the major critical element during pathological processes that are linked to the development of acute lung injury/acute respiratory distress syndrome (ALI/ARDS) and pneumonia. Despite this patho-physiological importance, little is known about the trauma-induced changes in the alveolar barrier.

There is evidence that trauma-induced ATP release is a key player in pulmonary dysfunction. The effects of ATP are mediated by purinergic signaling on target cells by P2Y or P2X receptors. Signaling via P2X receptors is known to modulate fluid transport and secretion of pulmonary surfactant, both important for maintaining alveolar homeostasis.

In my PhD project, I aim to establish *in vitro* trauma models of the alveolar barrier to reproduce indirect trauma insults (DAMPs, PAMPs). Combining the *in vitro* models with high-resolution techniques, I will study trauma-induced ATP release, activation of P2X receptors, fluid/ion and surfactant transport, and their influence on maintaining alveolar homeostasis following trauma on the cellular and molecular level.



Martin Wist

Born in 1990 in Göppingen, he completed his bachelor's and master's in Molecular Medicine at Ulm University (2009-2015). He joined the laboratory of Prof. Peter Gierschik at the Institute of Pharmacology and Toxicology for his master's thesis in 2014 and started to work on his PhD thesis there in 2015. Since October 2015, he has been a member of the International Graduate School in Molecular Medicine Ulm.

Rüstem Yilmaz

Born in Azerbaijan in 1987, he obtained his bachelor's degree in Molecular Biology and Genetics from the Middle East Technical University in Ankara, Turkey. After his master's in Molecular and Cellular Biology at Heidelberg University, he joined the Graduate School to pursue his PhD in Prof. Borck's group at the Institute of Human Genetics.

Functional characterization of deletions in the human gene encoding phospholipase C-γ_2 leading to cold-induced urticaria and immune dysregulation

Phospholipase C (PLC) enzymes are key regulators in cellular signalling. They catalyze the formation of the second messengers, inositol 1,4,5-trisphosphate (IP_3) and diacylglycerol (DAG), from the membrane phospholipid phosphatidylinositol 4,5-bisphosphate (PIP_2).
Deletions in the gene encoding the PLC isoform γ_2, predominantly expressed in hematopoietic cells, are associated with the novel human hereditary disease, PLAID (PLCγ_2-associated antibody deficiency and immune dysregulation), characterized by a rather puzzling concurrence of augmented and diminished functions of the immune system, such as cold urticaria triggered by only minimal decreases in temperature, autoimmunity, and immunodeficiency.
In previous experiments, we could show in intact cells that the PLAID PLCγ_2 deletion mutants are strongly (> 100-fold), rapidly, and reversibly activated by cooling by only a few degrees.
The aim of my PhD project is to further characterize the PLCγ_2 mutants both in intact cells and in vitro. In this way, we want to determine whether their cold temperature sensitivity is an intrinsic property of the mutant enzymes or relies on the interaction of the enzyme variants with regulatory proteins.

Genetic and functional analyses in blepharophimosis-mental retardation syndromes

Blepharophimosis-mental retardation syndromes (BMRS) are a clinically and genetically heterogeneous group of disorders that are characterized by intellectual disability, developmental delay, craniofacial features such as blepharophimosis, and various congenital anomalies. Biallelic mutations in *UBE3B* were reported in patients with Kaufman oculocerebrofacial syndrome (KOS), a type of BMRS. *UBE3B* codes for an uncharacterized E3 ubiquitin ligase. Elucidation of the role of UBE3B is essential for understanding the connection between mutations and the disorder. The aim of the thesis is to understand the pathophysiology and underlying molecular mechanism of KOS.

Arghavan Soleimani Zadeh

Born in 1986, she completed her BS and MSc studies in Iran. After obtaining her master's degree, she worked as a research assistant at the Pasteur Institute of Iran. In the summer of 2015, she was admitted to the International PhD Programme in Molecular Medicine at Ulm University. She is working on her thesis at the Institute of Biotechnology of Biberach University of Applied Sciences under the supervision of Dr. Katharina Zimmermann.

Malena Maria Zahn

Born in 1987, she studied Biology at the University of Regensburg in the field of Developmental and Cell Biology. She started her PhD at the Institute of Pathology to work in the field of classical Hodgkin's lymphoma.

Construction of vNAR libraries from cartilaginous fishes for the development of biopharmaceuticals and diagnostics

Monoclonal antibodies (mAbs) and their fragments are essential tools in basic research, diagnostics and therapy and cover a large market segment as cancer and immune therapeutics. Smaller antibody fragments become more and more relevant for therapy since they show improved tissue penetration, lower immunogenicity and reduced production costs. Moreover, such fragments can be used for targeted drug delivery that directs a drug cargo to a specific tissue or via the blood brain barrier (BBB). While conventional antibodies consist of two heavy and two light chains, with both chains contributing to the antigen-binding site, heavy chain antibody fragments consist of the antigen-binding site of the heavy chain only. Camelids (llamas, alpacas, dromedaries and camels) produce so-called heavy chain antibodies lacking the light chains. Cartilaginous fishes (sharks and skates) also produce the novel antigen receptor antibodies (IgNAR) composed only of a heavy chain. With biotechnological tools, the independent and highly stable binding domains can be expressed as small entities of 12–15 kDa, such as heavy chain fragments (VHH) derived from camelids or variable NAR (vNAR) derived from sharks. The small size and single domain format result in a considerably stable and easy production in heterologous expression systems. In this thesis, we aim to isolate derived antigen-specific IgNARs to construct antigen-specific libraries which are suitable for different biomedical applications. Therefore, we intend to establish a highly diverse semi-library with the Free University of Brussels (Vrije Universiteit Brussel). The libraries will be screened by phage display and, if needed, selected vNARs will be optimized by *in vitro* affinity maturation.

The impact of the tumor suppressor protein tyrosine phosphatase 1B (PTP1B) in the pathogenesis of classical Hodgkin's lymphoma

In my PhD thesis, I will focus on the tumor suppressor protein tyrosin phosphatase 1B (PTP1B) and its impact on the pathogenesis of classical Hodgkin's lymphoma (cHL). The JAK/STAT signaling will be of special interest for my project. This pathway is constitutively activated in cHL and the cHL cell lines (L428, L1236, UHO1…). PTP1B is a known negative regulator of this pathway, but its activity in cHL is very low. The downregulation of PTP1B could be due to a number of different reasons. For example, inactivation through phosphorylation, different mutations or the appearance of splice forms. We found some different shorter versions and I focused on one PTP1B variant which lacks the Exon 6. This variant appears to be a splice form of the wild-type protein with dominant negative effects. Furthermore, I will work on the AKT-mediated inhibitory phosphorylation of Ser50 in the active center of the PTP1B protein and will examine other signaling pathways, which are constitutively active in cHL, to investigate whether PTP1B has also some kind of impact on the activity or the target gene expression.

Verena Zoller

Born in 1987, she studied Biology at Ulm University. In April 2013. she started her PhD in the Division of Pediatric Endocrinology and Diabetes in the Department of Pediatrics and Adolescent Medicine. Currently, Verena is a member of the International PhD Programme in Molecular Medicine.

Lisa Zondler

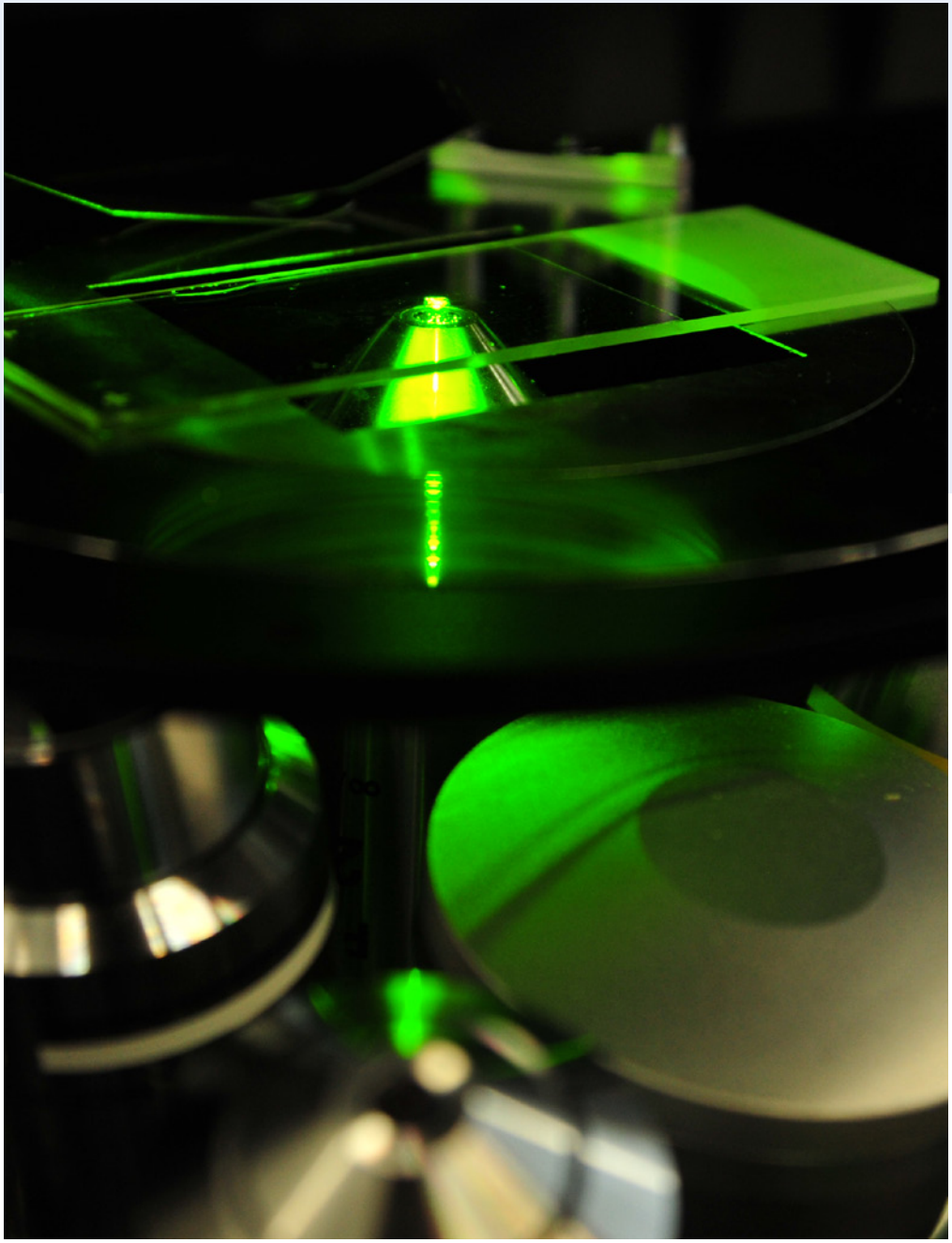
Born in 1987, I studied Molecular Medicine at Ulm University for both my bachelor's and master's. For my master's thesis, "The interplay of DJ-1 and a-Synuclein in Parkinson's disease," I moved to the Department of Neurodegeneration and Restorative Research, Göttingen. Currently, I am working on my PhD project, "Monocyte subpopulations in ALS," in the Department of Experimental Neurology, Ulm.

Regulation of adipose tissue homeostasis by the death ligand, TRAIL

The excessive accumulation of white adipose tissue (WAT) in obesity leads to severe comorbidities, such as type 2 diabetes mellitus, liver steatosis and cardiovascular disease, and also to an increased cancer risk. Weisberg et al. have shown that obesity is associated with an inflammation of adipose tissue as seen by the infiltration of macrophages. These immune cells, along with adipocytes and preadipocytes, are responsible for the production of cytokines and death ligands in adipose tissue. TNF-a and other members of the TNF superfamily affect adipose tissue metabolism and contribute to both the local and systemic obesity-associated inflammation. Our group studies the physiology and pathophysiology of obese adipose tissue. The aim of this PhD project is to understand the role of the death ligand, TRAIL (TNF-related apoptosis-inducing ligand), in adipocyte function. On the one hand, we study the influence of TRAIL on adipogenic differentiation with the aim of elucidating if it has a regulatory role on adipose tissue homeostasis. On the other hand, we investigate the impact of TRAIL on the secretory function of adipocytes. Adipose tissue is an important endocrine organ. We hypothesize that TRAIL contributes to the local inflammatory process and regulates the production of cytokines and chemokines.

Monocyte subtypes in amyotrophic lateral sclerosis

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease characterized by the progressive loss of motor neurons that results in the gradual failure of the neuromuscular system. So far, there is no cure and the underlying mechanisms of selective motor neuron vulnerability in ALS appear to be heterogenous among ALS patients. However, a common feature of all familial and sporadic forms of ALS is a massive neuroinflammatory reaction, including infiltration of peripheral immune cells into the central nervous system. The role of the peripheral immune system in this context remains controversial and, particularly, the function of myeloid cells in this context is not well understood to date. Therefore, the aim of my PhD project is to investigate the role of peripheral monocytes in both temporal and spatial dimensions of ALS pathogenesis.
To characterize functional abnormalities of peripheral ALS monocytes, we are using flow cytometry, isolation and culture of primary human monocytes, cell adhesion measurement and gene-expression analysis. To determine the number and appearance of infiltrated monocyte-derived cells in the central nervous system (CNS) of ALS patients, we are performing immunohistochemistry. To investigate the effect of immunomodulation on the monocytic system in ALS, we are treating ALS monocytes *in vitro* and ALS mice *in vivo* with different Fc-receptor stimulating agents by monitoring both their effect on disease onset and survival as well as the CNS infiltration and the behavior of peripheral monocytes.



Junior Faculty Projects

On the following pages, we present the projects of the members of IGradU's Junior Faculty.

Lisa Maria Cederlund

Born in 1977, I hold a master's in Chemical Engineering from Lund University (LTH), Sweden, and a PhD in Molecular Biology from University College Dublin, Ireland. I am currently working as a postdoctoral fellow in the group of Prof. Gilbert Weidinger at the Institute of Biochemistry and Molecular Biology.

A small molecule chemical screen to identify modulators of zebrafish bone regeneration

Unlike mammals, zebrafish have the remarkable ability to regenerate lost appendages. Fin regeneration proceeds through the formation of a blastema, a population of progenitor cells, which forms via dedifferentiation of mature osteoblasts. Such cellular plasticity is rare in adult vertebrates and very little is known about the molecular mechanisms regulating it. Thus, we aim to shed light on the molecular underpinnings of regenerative cellular dedifferentiation. We are using a library of small molecules with characterized targets to screen for compounds that block or enhance osteoblast dedifferentiation in adult fins *in vivo*. To facilitate the analyses, we are using transgenic reporter lines that allow us to follow osteoblasts at different stages of differentiation *in vivo*. Compounds with an effect on fin regeneration are linked to specific signaling pathways and studied in more detail using molecular methods.

priv.

Karin Danzer

Born on 28 November 1978, she is a junior professor and group leader in the Department of Neurology (Head: Prof. Albert Ludolph).

The underlying mechanisms of different neurodegenerative disorders with a special focus on Parkinson's disease

Aggregation of alpha-synuclein and related toxicities play a central role in the development of Parkinson's disease. Recently, oligomeric and pre-fibrillar forms of alpha-synuclein have been identified as the toxic species in Parkinson's disease. Until recently, alpha-synuclein was thought to exert its toxic effects intracellularly. However, new data support an alternative possibility that some forms of alpha-synuclein are secreted from, and taken up by, neurons and that this extracellular alpha-synuclein may be a toxic species. The goal of Dr. Danzer's research is to understand the underlying mechanisms of secretion, uptake of alpha-synuclein oligomers into neighboring neurons, and propagation of alpha-synuclein pathology. Her special interest is not only the exosomal secretion of alpha-synuclein oligomers but also additional key proteins in neurodegenerative disorders such as amyloid beta, Tau and SOD1. Using a wealth of biochemical, cell biological and molecular approaches, as well as the analysis of patient samples and establishing new animal models, Dr. Danzer hopes to understand the underlying disease mechanisms and to identify not only new biomarkers but also additional and new factors contributing to neurodegeneration.

Dr. Verena I. Gaidzik

Dr. Gaidzik works in the Department of Internal Medicine III (Head Prof. H. Döhner) as a clinical fellow. Her research projects take place in the research group of Prof. K. Döhner (Head of the laboratory for Cytogenetic and Molecular Genetic Diagnostics). Furthermore, she is mainly responsible for molecular genetic diagnostics in the laboratory.

Dr. Dr. Florian Kuchenbauer

I work as a physician in the Stem Cell Transplantation Unit in the Department of Internal Medicine III.

Molecular genetics in acute myeloid leukemia

The major focus of Dr. Gaidzik's research interest is to elucidate the underlying mechanisms of acute myeloid leukemia (AML) by identifying new genetic aberrations and by evaluating their prognostic and predictive relevance. Most of the scientific projects of Dr. Gaidzik are embedded in the framework of the prospective clinical AML trials of the German-Austrian AML Study Group (AMLSG). Thus, she has been able to analyze molecular markers, such as *WT1, RUNX1, TET2, DNMT3A*, in large patient cohorts with regard to their mutation incidence and discovered their associations with specific clinical and genetic characteristics. Furthermore, these studies aim to optimize the classification systems of AML patients and guide new and more specific treatment options. Another task is to improve the survival of AML patients by predicting and identifying patients with a high risk of relapse. This will be possible by investigating minimal residual disease (MRD) during therapy and follow-up. Currently, she works on the analysis of *DNMT3A* mutations as a new potential MRD marker. In the SFB 1074, "Experimental Models and Clinical Translation in Leukemia," she serves as a project leader and investigates a novel recurrent micro-deletion in the chromosomal band, 3p14.1-p13, which has recently been identified in AML patients.

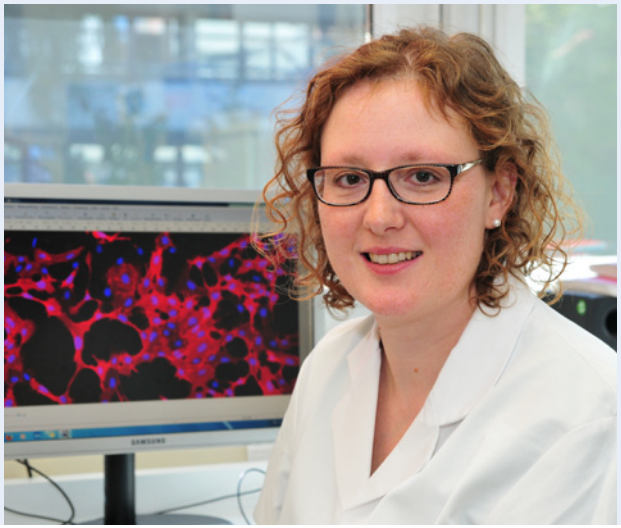
Mechanisms of lineage fate decisions in normal and aberrant hematopoiesis

My group explores mechanisms of lineage fate decisions in normal and aberrant hematopoiesis. We are interested in elucidating the molecular mechanisms and identifying novel genes involved in this process. Furthermore, we are investigating possibilities of reverting the block of differentiation in leukemic stem cells as potential therapeutic approaches. In addition, using various murine transplantation models, we are also interested in functional characterization of genetic driver lesions in acute myeloid leukemia (AML). Identification of novel leukemic drivers will lead to a better understanding of how leukemias arise and eventually result in new druggable targets. This involves coding and non-coding RNAs, such as microRNAs (miRNAs) and lncRNAs, which will be tested for their potential to manipulate hematopoietic as well as leukemic stem cells. Furthermore, we study upstream mechanisms regulating miRNA expression, including epigenetic modifications. Due to their highly stable nature, microRNAs have high potential as novel biomarkers. So far, treatment of medical conditions is in many cases symptom-oriented. In the case of malignant diseases, tumor markers, usually more or less specific circulating proteins, are used to monitor disease activity. However, for the majority of diseases neither markers for disease activity nor for therapy response are available. Therefore, we explore the potential of miRNAs in body fluids as biomarkers for malignant and non-malignant diseases.

priv.

Dr. Susanne J. Kühl (née Gessert)

In 1999, I began my studies in Biology at Ulm University and pursued my PhD from 2004 to 2007. Since then, I have been a postdoctoral researcher at the Institute of Biochemistry and Molecular Biology. In September 2015, I finished the Zertifikat für Hochschuldidaktik Baden-Württemberg and started my Master of Medical Education (MME) at Heidelberg University. I have written three textbooks, two of which are in the field of developmental and stem cell biology, and another on how to write a thesis.



Dr. Diana Lieber

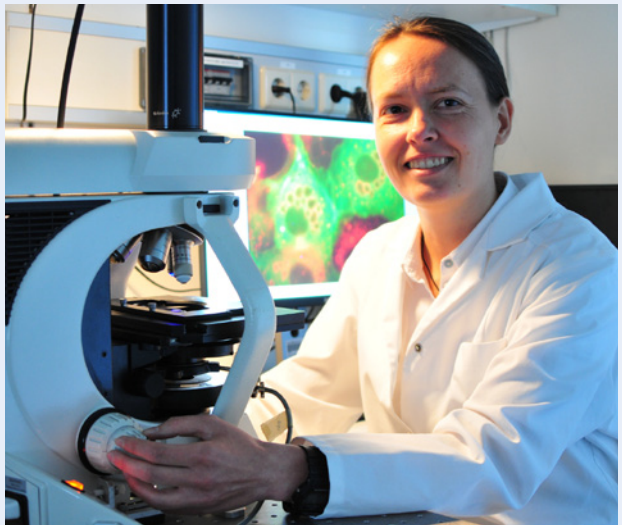
Born in 1976, I obtained my doctoral degree in Natural Sciences from the University of Freiburg in 2007. After a postdoctoral training program at the Ludwig Maximilian University of Munich, I joined the group of Prof. Christian Sinzger at the Institute of Virology in Ulm in 2011. Since 2013, I have been a member of the Junior Faculty of the International Graduate School in Molecular Medicine Ulm.

The analysis of non-canonical Wnt signaling during vertebrate kidney development

Wnt signaling is required for kidney development and misregulation of Wnt contributes to congenital kidney disease. We investigated the role of non-canonical Wnt target genes, Pes1 and Ppan, during *Xenopus* renal development (cf. Aleksandra Tata, a former PhD student of the IGradU; Tecza et al., Biol. Cell 2011). In a recent study, we analyzed alcam during embryonic kidney development (cf. Wiebke Cizelsky and Aleksandra Tata, former PhD students of the IGradU; Cizelsky et al., Development 2014). We showed that *alcam* is regulated by non-canonical Wnt signaling and that a loss of Alcam leads to abnormal tubule formation (Gessert et al., Dev. Biol. 2008; Cizelsky et al., Development 2014). Additionally, we showed that the potential non-canonical Wnt receptor, *fzd3*, acts upstream of *alcam* and that *alcam* is a direct target gene of non-canonical Wnt signaling. Our data set up a novel mechanism demonstrating a Fzd3/JNK/Alcam branch regulating embryonic kidney development. In cooperation with Seppo Vainio, Finland, we furthermore examined the regulation of *wnt4* by Wt1 and Sox11 on a transcriptional level (cf. Aleksandra Tata; Murugan et al., Exp. Cell. Rep. 2012). To gain further insight into the molecular mechanism underlying Alcam function, we are currently working on the characterization of direct Alcam interaction partners during early embryonic development (cf. Franziska Seigfried, a current PhD student of the IGradU).

Virus-host interactions during the initial stages of HCMV infection

Human cytomegalovirus (HCMV), a member of the family of herpes viruses, causes clinically inapparent infection in healthy individuals but resides life-long in the host. The viral persistence leaves the infected host at risk of severe disease under conditions of immunosuppression.
The main emphasis of my work lies in the identification of cellular factors that promote or impede virus entry into host cells. RNA interference is employed to explore focused sets of cellular genes in a systematic manner and to identify high-potential candidates. Successfully validated genes are characterized in the context of HCMV infection with regards to their molecular function and the affected infection step. With this as my aim, a broad range of virological methods and molecular biological technologies is employed, including knock-in and knock-out approaches. Different virus strains are included in the study to distinguish strain-specific from more general functions.
As a second research focus, cell-based reporter systems are established to quantitatively study HCMV infection *in vitro*. Well-established reporter genes are used to facilitate quantification of infection, while viral promoters with known expression kinetics are utilized to monitor the efficiency of the viral replicative cycle.
In all, my research aims to increase our understanding of the molecular interactions between HCMV and its host cell during the initial stages of infection, and to identify new targets for antiviral intervention.



Dr. Pika Miklavc

I studied biology at the University of Ljubljana in Slovenia and obtained a PhD in the field of neurobiology. I came to Germany as a Marie Curie Fellow of the European Commission and now work as a university assistant at the Institute of General Physiology in Ulm. Since 2013, I have been a member of the Junior Faculty of the International Graduate School in Molecular Medicine.

Dr. Astrid S. Pfister

I studied Biology in Erlangen and finished my diploma thesis in 2007 at the Institute of Experimental Medicine II, Erlangen. I continued there with my PhD and investigated the function of Amer2 in Wnt signaling. Since 2012, I have been working as a postdoctoral researcher at the Institute of Biochemistry and Molecular Biology in Michael Kühl's lab. In 2014, I joined the newly established Junior Faculty of the GradU.

Regulation of hemifusion and the post-fusion phase of exocytosis in alveolar type II cells

My research focuses on surfactant secretion in the lung alveolar epithelial cells. Secretory cells use regulated exocytosis, a specialized vesicular transport process, to release hormones, neurotransmitters or other substances into the extracellular space. Secretory material is stored in intracellular vesicles which fuse with the plasma membrane upon appropriate stimulation. Surfactant-secreting alveolar type II cells have large secretory vesicles and a slow sequential fusion process, which makes them an ideal cell model to study single vesicle fusion events in living cells by using high-resolution microscopy methods. The research encompasses hemifusion and post-fusion phases of exocytosis by focusing on regulation of vesicle content release after fusion pore opening. We could show that the actin cytoskeleton and calcium ions have a pivotal role in the later stages of exocytosis. Fused secretory vesicles in type II cells acquire actin coats, the compression of which enables surfactant release. In addition, influx of calcium through $P2X_4$ channels located on secretory vesicles contributes to fusion pore dilation and efficient surfactant extrusion. We are also interested in the pathological alterations of the secretory mechanism in type II cells and their implications for lung function.

Investigating the role of Wnt target genes in tumorigenesis

I study the cellular and molecular mechanisms underlying Wnt-mediated tumorigenesis. Wnt signaling regulates cell growth, proliferation and differentiation, and thus plays a crucial role in development and disease. Canonical Wnt ligands activate the Wnt/β-catenin pathway and drive the expression of Wnt target genes that regulate, for example, cell proliferation and apoptosis. Consistently, it has been demonstrated that several anti-apoptotic Wnt targets are up-regulated in tumors with constitutively active Wnt signaling, for instance, in colon cancer and leukemia. Thus, I focus on anti-apoptotic Wnt target genes by molecular biological methods and *in vitro* cell-culture assays on primary, cancer and acute myeloid leukemia (AML) cell lines. Moreover, I investigate the *in vivo* function of interesting candidates in *Xenopus laevis* as a potent model organism (Pfister et al., 2012). My current research concentrates on the Wnt target nucleophosmin (NPM), which is commonly mutated in AML patients and on its interaction partner Peter Pan (PPAN). Both are crucial ribosome biogenesis assembly factors and important for cell survival. So far, we could show that PPAN knockdown triggers mitochondrial apoptosis, reduces NPM levels and triggers nucleolar stress (Pfister et al., 2015). In contrast, PPAN overexpression made cells more resistant to treatment with chemotherapeutic agents. In our ongoing projects, we are analyzing the role of these factors in more detail. Besides this, we will also screen for novel candidates that are relevant for tumor biology.

Michael J. Schmeisser

Dr. med. Dr. rer. nat. Michael J. Schmeisser was born on 2 June 1983 in Kempten, Allgäu. He is leading a junior research group at the Institute for Anatomy and Cell Biology (Head: Prof. Dr. med. Tobias Böckers). Currently, he is a participant in the Neurology Residency Program at Ulm University Hospital (Head: Prof. Dr. med. Albert Ludolph).

Translational neuroanatomy of neuropsychiatric disorders

The current research focus of Michael's group is translational neuroscience. With students rom diverse backgrounds that include Medicine, Molecular Medicine, and Biology, Michael wants to understand the biological mechanisms of neurological and psychiatric disorders. In this context, he is very interested in neural development and its relation to disease. Most of his current work focuses on mouse models and molecular pathomechanisms of autism spectrum disorders. His further projects address the possible pathomechanistic overlap of aberrant neurodevelopment and neurodegeneration. Due to his clinical assignment, he wishes to translate his findings in the lab directly to the treatment of patients in the future.

In recent years, he has been a guest scientist at the Institut Pasteur in Paris and the CNR Institute of Neuroscience in Milan, and has won several awards for his research. He has also established a vibrant international network of junior scientists that include colleagues from Ulm, Mainz, Magdeburg, Paris, Milan, London, Utrecht, Klosterneuburg/Vienna, Beijing and Melbourne.

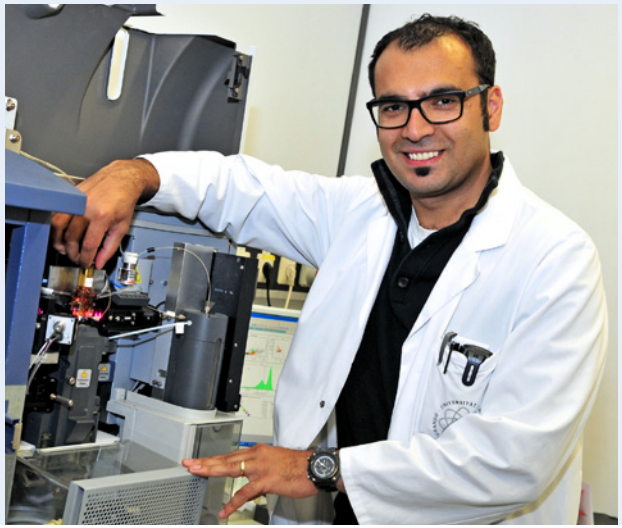
Apart from his research activities, Michael loves teaching students in anatomy and neuroscience. He is board-qualified as an anatomist and holds the Teaching Certificate of the state of Baden-Württemberg.

Christoph Schmidt

Born in 1978, he is a junior group leader and a member of the scientific staff at the Institute of Pharmacology of Natural Products and Clinical Pharmacology. Christoph also joined the Junior Faculty of the International Graduate School in Molecular Medicine Ulm (IGradU). For more information, please see the laboratory homepage: www.applied-immunology.com

Opsonization by the innate immune system: understanding the delicate balance between normal function and pathophysiology sets the stage for novel immune-modulating applications

My group's interest lies in innate immunology by especially focusing on the protein defense network of the complement system. We are particularly interested in the process of opsonization by the innate immune system. Complement opsonins not only mark pathogens but also cellular waste and debris for efficient disposal. Depending on the activation profile of the complement cascade, the process of complement opsonization can generate or prevent the release of strong inflammatory signals. Both too much or too little complement activation can cause or worsen many rare and common human diseases. We investigate, on a molecular and a cellular level, how this delicate balance is maintained or destabilized. Additionally, we engineer and produce novel immunomodulatory complement inhibitors that we subsequently test (in collaboration) in clinically relevant *ex vivo* models on patient material or in animal models of complement-mediated diseases.



Alpaslan Tasdogan

I was born in the eighties and raised in the nineties. I studied Molecular Medicine and Human Medicine at Ulm University. Currently, I am a clinician scientist in the Department of Dermatology and work at the Institute of Immunology. The unique advantage of being a clinician scientist is the possibility of being involved in all aspects of translational medicine, including "bench-to-bedside" medicine.

Dissecting hematopoietic defects in Mixed-lineage-Leukemia-5-deficient mice and cell lines

Mixed Lineage Leukemia 5 (MLL5) is a distant and understudied member of the MLL/Trithorax gene family of epigenetic regulators. Classical members of this family (MLL1 – MLL4) are known to exhibit histone H3K4 methyltransferase activity and to be critically involved in normal hematopoiesis as well as hematopoietic malignancies. Along this line, human MLL5 is located in a genomic region (chromosome 7q22) recurrently deleted in leukemic cells from patients with aggressive forms of acute myeloid leukemia (AML). This initial observation has given rise to the view that MLL5 might exhibit tumor-suppressor activities. The analysis of adult MLL5-deficient mice, generated in our own and two other laboratories, has revealed a variety of phenotypic abnormalities, including infertility, retarded growth and severe defects in hematopoiesis, which is a combination of traits often found in mouse mutants with defective DNA double strand break repair. Moreover, hematopoietic stem/progenitor cell compartments were severely compromised functionally. However, molecular studies of MLL5 function are still scarce and no direct experimental evidence for a pathogenic role of MLL5 has yet been reported.

Organization of the Graduate School

Who we are - Organization of the Graduate School

The International Graduate School in Molecular Medicine Ulm is an interdisciplinary central institution of Ulm University headed by a Board of Directors consisting of a chairman, a vice chairman, a representative of the presidency of Ulm University, a representative from the Faculty of Natural Sciences, and a managing director. The Board of Directors is responsible for the scientific profile of the Graduate School, the interdisciplinary training, the regulation of programs, the performance-based allocation of resources, and public relations. While the chairman acts as the representative of the Graduate School, the managing director is responsible for the school's administrative management. Both are official representatives of the Graduate School in financial affairs. The board decides on all financial issues concerning the Graduate School, such as work contracts, mobility programs, and applications for the various social programs on offer.

The Board of Directors is supported by an International and Scientific Advisory Board which offers suggestions for the general development of the Graduate School and its PhD program. The Advisory Board includes scientists from Ulm University's various faculties in addition to those from other national and international research institutes and universities, as well as representatives from pharmaceutical companies. While the scientific members ensure the international compatibility of the PhD program and its compliance with international standards, the representatives from industry offer advice that is particularly relevant to the employability of our PhD graduates.

Members of the International and Scientific Advisory Board (November 2015):

Academic Representatives	Industrial Representatives	Representatives of Ulm University	Alumni of the Graduate School	Student Representatives
D. Brockmann, Managing Director of IGradU	U. Bücheler, Boehringer Ingelheim	P. Dürre, Dean of the Faculty of Natural Sciences	M. Dittmann, New York, USA	B. Kozak, Institute of General Zoology and Endocrinology
J. Hannemann, Biberach	N. Rentschler, BioRegionUlm	A. Huckauf, Equal Opportunities Commissioner, Institute of General Psychology		S. Reichel, Institute of Physiological Chemistry
M. Kühl, Chairman of IGradU	H. Wendt, CEFIC, Belgium	D. Rautenbach, Dean of the Faculty of Mathematics and Economics		S. Rode, Institute of Molecular Virology
S. A. Moody, Washington, USA		T. Seufert, Dean of the Faculty of Engineering, Computer Science and Psychology		
P. Pozzilli, Rome, Italy		T. Wirth, Dean of the Medical Faculty		
M. Thelen, Bellinzona, Switzerland				
S. Vainio, Oulu, Finland				

The PhD Committee is in charge of the scientific monitoring and development of the *International PhD Programme in Molecular Medicine* right from the start of the application procedure through to the thesis defense. It is responsible for the assessment of applications in order to maintain the high standards of research required by the program. Furthermore, the PhD Committee supervises the school's compliance with the regulations of the program and constantly improves them. It also conducts the intermediate evaluations as well as the disputation of students. The PhD Committee consists of eight scientists from Ulm University and one student representative.

The Principal Investigators (PIs) are a group of 41 scientists from Ulm University responsible for the scientific profile and organization of the Graduate School as well as for the training of our PhD students. For instance, the PIs organize the six different Research Training Groups of the Graduate School. In addition to this, each Thesis Advisory Committee (TAC) includes at least one PI to ensure equal and excellent standards of research training for all PhD students.

As mentioned previously, doctoral students are organized and trained in smaller **Research Training Groups** from the beginning of their PhD studies. The groups concentrate on different research topics of Molecular Medicine and each group includes a number of Principal Investigators responsible for its coordination.

The six Research Training Groups are: 1) Development and Regeneration, 2) Oncology, 3) Aging, 4) Neurobiology, 5) Host-Microbe Interaction, and 6) Trauma Research.

Moreover, highly proficient medical students are trained in clinical research by participating in the "Programme of Experimental Medicine."

Due to the increasing number of PhD students and students entering the *Programme of Experimental Medicine*, **the Coordination Office** consists of four coordinators responsible for the administration and organization of the Graduate School. They are the principal contact point for all students, supervisors and applicants, and give advice and support concerning Graduate School policies and procedures, as well as answering questions concerning academic issues. The office also preselects applications and coordinates the selection procedure. The organization of curricular and extracurricular activities as well as meetings and examinations are all part of the daily work of the Office. The handling of the Graduate School's public relations is also one of its duties. In addition, they coordinate the smooth interaction and cooperation between the large number of people and institutions involved in the Graduate School.

How to study the *International PhD Programme in Molecular Medicine*

During the three-year period of PhD studies, students must take part in a number of compulsory seminars and activities. Central teaching activities include the lecture series *Improve your Textbook Knowledge* for first and second year PhD students as well as the participation in a *Journal Club* and the biweekly seminar *Progress Report*. The lecture series *Improve your Textbook Knowledge* allows graduates from different disciplines to refresh the basic knowledge needed to perform research in Molecular Medicine independently of their scientific background.

In the seminar *Progress Report*, students are trained to communicate and present their own research data to their fellow students and to place it in a broader international context. Furthermore, graduates must attend a series of 30 lectures a year presented by external speakers. Another important compulsory course is the seminar *Good Scientific Practice* which takes place before the start of any practical work. All students have to present a project plan within the first six months of their PhD studies. This helps the students and supervisor to structure their project, set objectives and establish a career plan.

In addition to curricular seminars and lectures, we offer PhD students a large variety of optional activities. As one of our aims is to give students an insight into the work of industrial employers, we arrange excursions to pharmaceutical and biotech companies. Summer schools and other scientific events in cooperation with partners from industry help to motivate students to deepen their knowledge of basic science and R & D. We also organize annual scientific retreats focusing on particular topics, for example, *Advanced Concepts in Molecular Medicine* held at Lake Como, Italy, in May 2015. Also in 2015, the joint PhD Program with the University of Oulu held its third retreat in November in the city of Oulu. Furthermore, there is a wide range of key competence seminars organized in order to improve the employability of our graduates. For instance, we offer courses in biosafety, bioethics, project management, funding, patent rights, copyright law, scientific writing and presentation, team work and leadership skills, and career workshops.

From a wide variety of optional activities, students must choose a minimum of two courses per year. Within the first two years of doctoral training, students are expected to attend two practical courses in different national laboratories or abroad over a period of ten days. This practical training allows graduates to learn new and innovative techniques in Molecular Medicine.

International PhD Programme in Molecular Medicine – Study Plan

First study year

1.1	Lecture Series I (30 optional talks)***
1.2	Journal Club I* (1.5 hrs / 2 weeks)
1.3	Seminar Progress Report I (weekly)
1.4 1.5	Lecture “Improve your textbook knowledge”** Seminar “Good Scientific Practice”
1.6 1.7 1.8	Project Plan: within the first 6 months, length 3-6 pages Participation in the Spring and Fall Meetings of the Graduate School***** One additional optional activity (8 hrs, e.g. minisymposia, excursions, workshops, etc.)***

Intermediate Evaluation 1 ***

Second study year

2.1	Lecture Series II (30 optional talks)***
2.2	Journal Club II* (1,5 hrs / 2 weeks)
2.3	Seminar Progress Report II (weekly)
2.4 2.5	Compulsory optional practical training**** Participation in the Spring and Fall Meetings of the Graduate School*****
2.6	Two additional optional activities (8 hrs each, e.g. minisymposia, excursions, workshops, etc.)***

Intermediate Examination 2 ***

Third study year

3.1	Lecture Series III (30 optional talks)***
3.2	Journal Club III* (1,5 hrs / 2 weeks)
3.3 3.4	Seminar Progress Report III (weekly) Participation in the Spring and Fall Meetings of the Graduate School*****
3.5	Two additional optional activities (8 hrs each, e.g. minisymposia, excursions, workshops, etc.)***

PhD project work

Particular elements of our study concept are also included in two intermediate symposia which take place for a public audience in April and October each year. Students must pass evaluations at the completion of their first and second year of study to ensure proper progress in their chosen scientific project. Both evaluations take place within a public forum at our international meetings. While the first intermediate evaluation consists of a poster presentation before the Thesis Advisory Committee (TAC), the second intermediate evaluation includes a scientific talk in addition to a poster presentation. Only those students who successfully pass may proceed to their second or third year of study.

According to the study regulations updated in 2015, the evaluations are graded as “passed” or “not passed.” The final grade of the PhD-thesis is composed of the grades of the dissertation and disputation.

Supervision Agreement

It is the mission of the Graduate School to provide excellent and guaranteed supervision for every PhD student participating in the program. Therefore, the Board of Directors has decided that each individual student, together with each member of the TAC, must sign a supervision agreement within the first six months of the PhD Programme. The purpose of the supervision agreement is to define the rights and duties of the students, the Thesis Advisory Committee and the Graduate School respectively. The aim is to protect each party in this supervision arrangement.

As a rule, regular attendance is at 85% of the planned courses per year. This rule explicitly does not apply to the “Good Scientific Practice” seminar, for which no absences are envisaged.

*The “Journal Club” should be attended at the institution of the first or second supervisor. A participation confirmation in the Journal Club must be submitted for the first and second intermediate examination, as well as for the submission of the dissertation.

**For the “Improve your textbook knowledge” lecture, regular attendance constitutes 85% participation in this course. The required sessions can be attended within two years.

***For admission to the intermediate examinations and the dissertation, an appropriate list of participants and a list of attended activities must be submitted four weeks prior to the relevant examination and the submission of the dissertation.

****The “Practical Training” courses take a total of 10 working days in two different laboratories and must be completed prior to the 2nd intermediate evaluation. They are not permitted to be held in the institution of the first supervisor. A participation confirmation must be submitted in accordance with the aforementioned time periods.

*****Once per year, the Graduate School holds a spring congress and an autumn congress, at which intermediate evaluations are carried out. For PhD students who are not required to take intermediate evaluations, it is nevertheless compulsory to attend and participate in the events. The PhD Committee will regulate any exceptions.

How to apply

Does the study concept of our international PhD program attract you? The following information will advise you about our application and selection procedures as well as the funding of PhD positions.

Our PhD Selection Procedure

The Graduate School accepts new students for the PhD program in April and October each year. The formal admission requirements are:

- A Master of Science degree, a German state examination or an equivalent degree in either the life sciences, physics, chemistry, informatics or a related field.
- An overall grade of 2,0 or above according to the German grading system.

Applicants who meet with our formal admission criteria are invited to our PhD Selection Days. During these days, applicants give an oral presentation in English on the topic of their master's thesis and are personally interviewed by representatives of the Graduate School. They also have the opportunity to meet the project leaders of the PhD projects they have applied for.

Following our PhD Selection Days, applicants will be admitted to the PhD program on condition that:

- The candidate's oral presentation and the personal interviews have been evaluated with an overall grade of 2,0 or above according to the German grading system.
- The applicant has demonstrated above-average English language skills during the presentation and the personal interviews.
- A potential supervisor has given a written statement accepting the applicant as a PhD student.

How to find a PhD Project

These are the most convenient ways to choose a PhD project at Ulm University:

- Respond to one of the advertisements on our homepage (http://www.uni-ulm.de/einrichtungen/mm/phdprogramme/application/phdpositions.html) or to those published twice a year in the magazine, *Nature*, and also *Die Zeit*.
- Establish contact with a professor from Ulm University who is willing to accept you for a vacant PhD position.

Application

If you wish to apply for our PhD program, you must use our online-application platform (https://gs-molmed-uni-ulm.de/campuscore/application/views/introView.page).
During the application process, you will be asked to provide the following documents:

- Academic transcripts (bachelor's certificate, master's certificate, transcript of records, diploma supplements etc.)
- A curriculum vitae outlining your previous education and professional experience

Important remarks

- Submitted documents must be in PDF format.
- All submitted documents must be provided either in English or in German. If original documents are neither in English nor in German, certified translations are required.
- Applicants who are invited to our PhD Selection Days can request financial support to cover part of their travel costs.
- The personal presentation at Ulm University is part of our selection procedure and cannot be replaced by telephone or Skype interviews.
- Please note that applicants who succeed in our PhD Selection Days can only be accepted for the PhD program if they have been accepted for a PhD position by the Graduate School or by a supervisor from Ulm University.

How to finance a PhD position

Acceptance into our PhD program and securing a PhD position at Ulm University do not automatically mean that you will receive funding from Ulm University. We ask that you make arrangements in advance to ensure that your PhD position will be financed. The following options are possible:

- Receive a work contract from the Graduate School
- Gain acceptance for a paid PhD position through a professor of the University
- You can also finance yourself either through a scholarship from your home country, from DAAD, or from any other funding organization.

The Graduate School's work contracts amount to a salary of approximately €1,400 per month (after tax). If you are not funded by the Graduate School, your salary may differ from this amount due to an alternative way of financing. Please ask your supervisor or your funding organization about the monthly income rate.

Please note:
There are no tuition fees for doctoral students at Ulm University.

Guidelines of the International Graduate School in Molecular Medicine Ulm

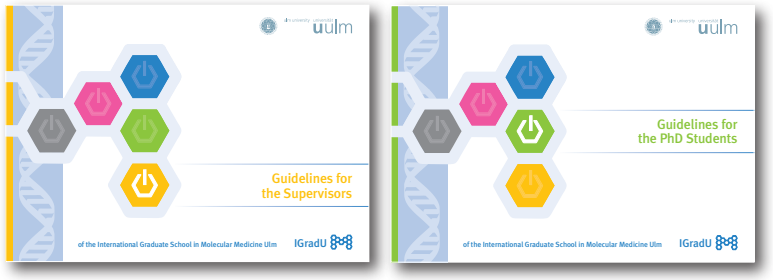
In order to assist doctoral students during their thesis, the Graduate School has published five guidelines summarizing the most important rules of both study programs. These guidelines also describe the tasks of supervisors who train and educate PhD students of the Graduate School. Our guidelines deal with Good Scientific Practice and Good Supervision Practice. They also describe the milestones of a PhD thesis for doctoral students and their Thesis Advisory Committees. Finally, a specific guideline has been written for medical students participating in the program Experimental Medicine.

Good Supervision Practice

Based on a workshop followed by in-depth discussions between PhD students and supervisors, the Graduate School has defined standards for good supervision practice. Good supervision of PhD students requires sufficient time made available with the supervisor and depends on the comprehensive interaction of both parties. Students must be empowered to carry out their projects in a self-responsible manner. Motivation, enthusiasm, curiosity and diligence will help in taking on and dealing with the demands of a doctoral degree.

Good Scientific Practice

The academic world of science has recently had to tackle the issue of falsification and plagiarism. Scientific misconduct can range from the copying of full texts to such cases that are judged scientifically unethical. Consequently, this emphasizes the need for students to be reassured of what constitutes good scientific work and for individual scientists to make themselves familiar with the rules. These guidelines are intended to give our students a brief overview of what is good scientific practice and how to prevent scientific misconduct.



Guidelines for the Supervisors

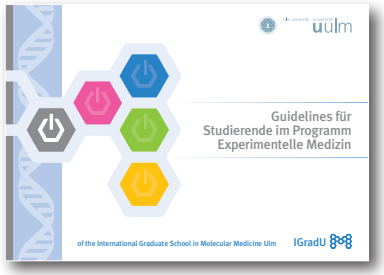
It is the role of supervisors to be available to help graduate students at every stage of their doctoral research. To assist in managing this challenge, the Graduate School has developed guidelines for supervisors to define several of their required duties and to respond to issues that may arise for supervisors at the Graduate School.

Guidelines for PhD Students

This guideline contains all the necessary information regarding the obligations and benefits of the structured PhD program so that students can successfully fulfill all the requirements to obtain a PhD or Dr. rer. nat. degree and to prepare themselves for a career in academia and industry.

Experimental Medicine

The structured training program, *Experimental Medicine*, was adopted by the Graduate School in 2009. This guideline defines both the rules for doctoral students participating in this particular program as well as their duties, among which are included scientific presentations of their work in a seminar series. The Medical Faculty and IGradU support this program with up to 35 stipends yearly.



Ulm University and Science City

Founded in 1967, Ulm University is the youngest university in the state of Baden-Württemberg. From the beginning, the *College of Medicine and Natural Sciences* had a clear focus on the disciplines the name suggests: biology, chemistry, physics, mathematics and medicine. This was how the original range of subjects looked. The founders explicitly attributed to this new institution of advanced education the character of a research university. The close contact among different subjects and the interdisciplinary character of research were encouraged and promoted. This concept of a “university under one roof ” has been maintained over the years and has been exercised in the hiring of professors. Faculties have always ensured that the areas central to the work of new professors and of those who are already employed by the university continue to progress. This idea is the basis for concentrating on certain fields of research and the foundation of a series of collaborating research centers established at Ulm University over the years.

The university's excellent reputation is largely due to the high level of cooperation among the different disciplines. Many research awards and commissions for cooperation projects, whether in the fields of computer science, economics, engineering and mathematics, or the natural and life sciences, are proof of this.

Since the university's foundation, the original range of disciplines has been enlarged. At present, Ulm University consists of four faculties: Natural Sciences; Engineering, Computer Science and Psychology; Mathematics and Economics; and Medicine. It hosts more than 10,000 students. Ulm University is renowned for its personalized atmosphere and for the close working relationship that exists between its students and professors. Its research profile is characterized by a focus on the life sciences and medicine, quantum science and technology, energy conversion and storage, cognitive systems and human computer interaction, financial services and their mathematical methods. Further specialized areas, such as pharmaceutical biotechnology as well as a bachelor's course of study in Psychology, have been established in recent years.

The main university campus is located on a hill above the city of Ulm (*Eselsberg*) and houses a wide range of research and development centers as those of Daimler, BMW, Audi, Continental, AEG MIS as well as such research institutes as IDT (Institute for Diabetes Technology), ILM (Institute for Laser Technology in Medicine and Measurement Technique), ZNL (Transfer Center for Neuroscience and Learning) and ZSW (Centre for Solar Energy and Hydrogen Research Baden-Württemberg) among others. In addition, there are several hospitals that together comprise what is known as the Science City or *Wissenschaftsstadt*. This proximity of academic institutions and industrial R&D allows improved interaction between academic teaching and research on the one hand and industrial needs on the other.

Situated between woods and grain fields, the campus offers space for recreation and an outstanding view over the city. The art trail known as the *Kunstpfad* exhibits the artworks of internationally renowned and talented young artists distributed throughout the campus.

About the City of Ulm

Ulm/Neu-Ulm is an attractive twin city lying at the heart of southern Germany between Stuttgart and Munich. The 178,144 citizens of Ulm and Neu-Ulm are divided between the two states of Baden-Württemberg and Bavaria by the river Danube. The two municipal authorities cooperate and have grown into a common economic area. As the commercial and cultural heart of the region, they act in unanimity. Both cities have excellent traffic connections with the north-south and the east-west highways, six railway lines and five major state roads all intersecting here. Ulm's main train station is situated on an important rail route. The nearest airports are located in Stuttgart (approx. 80 km/50 miles) and Munich (approx. 145km/90 miles).

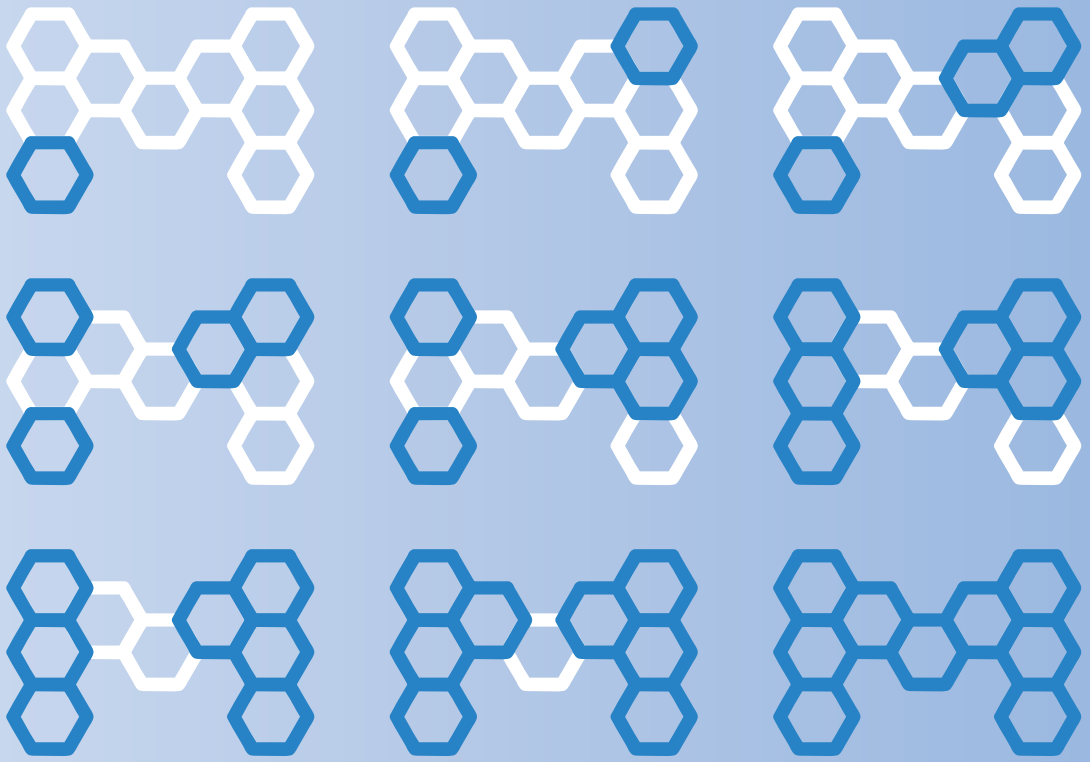
While Ulm is an ancient town, Neu-Ulm is relatively young. In Ulm, there are the charming Fisherman's and Tanners' Quarter with its old houses, alleyways and that air of medieval times. In Neu-Ulm, regularity in its architecture prevails since this was the only form considered to be stylish and elegant in the 19th century. Neu-Ulm was originally established as a counterpart to Ulm. Today, the two sister cities, though unlike, are both open to contemporary ideas of construction. The city center of Ulm houses a mixture of stone monuments from its days as a free city of the Holy Roman Empire and more

recently designed modern architecture, for example, the postmodern townhouse next to the gothic minster and the historical market place with its city library in the form of a glass pyramid. Neu-Ulm has also come a long way with the modernization of its city center.

The twin city of Ulm/Neu-Ulm offers a large variety of cultural events such as the *Museumsnacht* (Night of the Museums), *Internationales Donaufest* (International Danube Festival) and the *Ulmer Zelt*, one of many music festivals. There is a main theater as well as several other smaller theaters. Whether sociable or fashionable, there are bars, pubs, cafés and beer gardens to suit everyone's taste. The city's geographical proximity to the Allgäu, Lake Constance and the Alps offers the opportunity to enjoy sporting activities such as hiking, cycling, skiing and surfing. So it is no surprise that in an attractiveness survey conducted by Immakomm, Ulm reached fourth rank in 2014 and, in the same year, the city achieved the greatest increase in tourists in Baden-Württemberg, an increase that was greater than that of such cities as Heidelberg and Tübingen. A survey by IHK Ulm (*Industrie- und Handelskammer Ulm*/Chamber of Commerce and Industry, Ulm) has shown that the region of Ulm has the highest economic growth in Germany and that the local economy expanded by an impressive 44 per cent between 1996 and 2009. Despite the economic crisis in Europe and around the world, Ulm's economy and population still managed to grow further and a mere three per cent of Ulm's citizens are currently out of work. It is in this context that Ulm has been declared as Germany's *Wohlfühlregion Nr. 1* (Feel-good-region no. 1) in a survey by Deutsche Bank and is, according to IW Consult (2014), a role model in its economic development.

The Ulm region called *Stiller Star* (Silent Star) by the German newspaper *Handelsblatt* is an important center for the pharmaceutical industry and biotechnology. While Ulm's general economy is already placed among Germany's top ten cities (*Institute der Deutschen Wirtschaft 2013*), the pharmaceutical industry and biotechnology are the fastest growing and leading industries in Germany and Europe, and include large corporations such as Boehringer Ingelheim (a world leader in biopharmaceutical contract manufacturing), Rentschler Biotechnologie, TEVA/Ratiopharm, Cognis. They are all located here in Ulm and attest to the close interaction between the world of science and the economy.

"Sehnsucht und Weitblick" was the motto of the 125th anniversary of the completion of Ulm Cathedral's steeple in 2015. The lettering mounted on the rooftop of the Stadthaus, which was built by the New York-based architect Richard Meier, breathes optimism into the life of the city, its inhabitants and visitors



Facts and Figures

Facts and Figures

(as of January 2016)

PhD Students, *International PhD Programme in Molecular Medicine*

Total number of PhD students	205
Male	65
Female	140
International students	48
Parental students	9

PhD Students, *Programme in Experimental Medicine*

Total number of PhD students	48
Male	24
Female	24
International students	2
Parental students	0

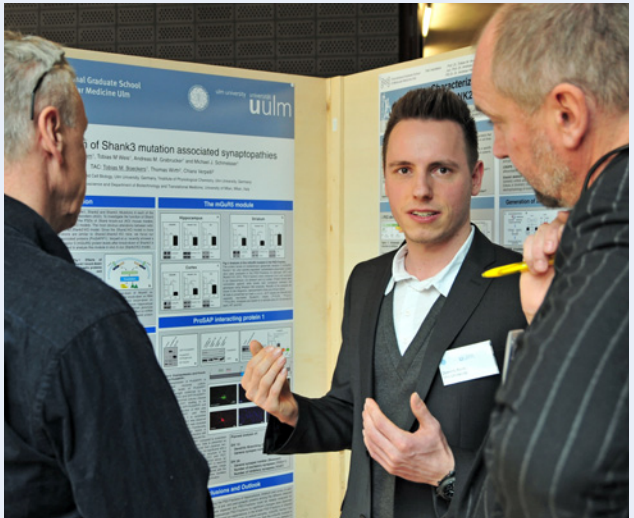
Doctorates conferred (2013-2016), *International PhD Programme in Molecular Medicine*

Name	Topic	Main supervisor (names)	Institute	Date of final examination	Degree
Sagar, Anubha	Role of S agalactiae ß-Hemolysin and S pneumoniae choline in their interactions with the cells of the innate immune system	Prof. Dr. Spellerberg, Barbara	Institute of Medical Microbiology and Hygiene	28.2.2013	PhD
Enzenmüller, Stefanie	PI3-Kinase inhibition primes cancer cells for lysosomotropic agents	Prof. Dr. Fulda, Simone	Department of Pediatrics and Adolescent Medicine	2.7.2013	Dr. rer. nat.
Schmeisser, Michael Joachim	The role of NF-kappaB and Insulin-like growth factor signaling in the formation of synapses	Prof. Dr. Böckers, Tobias	Institute for Anatomy and Cell Biology	17.7.2013	Dr. rer. nat.
Dorneburg, Carmen	Notch in the molecular pathogenesis and therapy of neuroblastoma	Prof. Dr. Beltinger, Christian	Department of Pediatrics and Adolescent Medicine	31.7.2013	Dr. rer. nat.
Lillich, Maren	Application of Clostridium botulinum C3 toxin for targeted delivery of proteins and viruses into macrophages	Prof. Dr. Barth, Holger	Institute of Pharmacology and Toxicology	7.8.2013	Dr. rer. nat.
Arnold, Franziska	Role of amyloid fibrils in HIV transmission and infection of the brain	Prof. Dr. Münch, Jan	Institute of Molecular Virology	13.9.2013	Dr. rer. nat.
Schneider, Clemens	Involvement of the bud neck localized protein Bni5 in the assembly of myosin and septin higher-order structures in Saccharomyces cerevisiae	Prof. Dr. Johnsson, Nils	Institute of Molecular Genetics and Zoology	18.9.2013	Dr. rer. nat.
Bischof, Joachim	Identification of Chk1 as CK1 delta targeting kinase and validation of new CK1 isoform-specific inhibitors	apl. Prof. Dr. Knippschild, Uwe	Department of General and Visceral Surgery	19.9.2013	Dr. rer. nat.
Linta, Leonhard	Human Induced Pluripotent Stem Cells – A powerful tool for in vitro research	Prof. Dr. Böckers, Tobias	Institute for Anatomy and Cell Biology	24.9.2013	Dr. rer. nat.
Cizelsky, Wiebke	Transcriptional regulation and functional characterization of Alcam during Xenopus laevis embryonic development	Prof. Dr. Kühl, Michael	Institute of Biochemistry and Molecular Biology	30.9.2013	Dr. rer. nat.
Prill, Jan-Michael	Towards systemic vector delivery: Studies on the role of position-specific hexon shielding of adenovirus type 5-based gene transfer vectors	Prof. Dr. Kochanek, Stefan	Department of Gene Therapy	2.10.2013	Dr. rer. nat.
Qi, Yu	Characterisation of the effect of MSCs on macrophage activation in chronic wounds	Prof. Dr. Scharffetter-Kochanek, Karin	Institute of Dermatology and Allergic Disease	9.10.2013	PhD
Edmaier, Katrin	Dissecting the Role of Lef-1 in Normal Hematopoiesis	Prof. Dr. Buske, Christian	Institute of Experimental Cancer Research	18.11.2013	Dr. rer. nat.
Hartmann, Daniel	Telomerase gene mutations are associated with cirrhosis formation	Prof. Dr. Rudolph, Karl Lenhard	Department of Molecular Medicine	22.11.2013	Dr. rer. nat.
Schmidt, Thomas	Induction and phosphorylation of the small heat shock proteins HspB1/Hsp25 and HspB5/AB-crystallin in the rat retina after optic nerve injury	Prof. Dr. Golenhofen, Nikola	Institute for Anatomy and Cell Biology	6.12.2013	Dr. rer. nat.
Brock, Ivonne	Involvement of the multivesicolar body biogenesis in the herpesviral life cycle	Prof. Dr. Mertens, Thomas	Institute of Virology	11.12.2013	PhD
Kleinhans, Karin Nena	The role of the Bloom's Helicase during aging, at dysfunctional telomeres and after DNA damage	Prof. Dr. Rudolph, Karl Lenhard	Department of Molecular Medicine	10.1.2014	Dr. rer. nat.
Steinestel, Konrad	The role of Abelsoninteractor 1 (Abi1) In colorectal carcinoma	Prof. Dr. Möller, Peter	Institute of Pathology	7.2.2014	Dr. rer. nat.

Name	Topic	Main supervisor (names)	Institute	Date of final examination	Degree
Guo, Yanchun	Functional analysis of Dkk1 and Mef2 during early cardiac development in Xenopus laevis	Prof. Dr. Kühl, Michael	Institute of Biochemistry and Molecular Biology	25.2.2014	PhD
Bayer, Carina	Infection of macrophages with human cytomegalovirus (HCMV): Analysis of antigen presentation	Prof. Dr. Mertens, Thomas	Institute of Virology	5.3.2014	Dr. rer. nat.
Rossini, Valerio	CX3CR1+ Antigen presenting cells of the Lamina Propria Activate CD4 T cells during transfer colitis	Prof. Dr. Niess, Jan-Hendrik	Clinic for Internal Medicine I	12.3.2014	PhD
Fan, Chunxiang	Transient compartment-like syndrome and normokalemic periodic paralysis due to a Cav 1.1 mutation	Prof. Dr. Lehmann-Horn, Frank	Divison of Neurophysiology	16.4.2014	PhD
Führer, Marita	Molecular pathophysiology of (severe) combined immunodeficiency	Prof. Dr. Schwarz, Klaus	Institute of Transfusion Medicine	14.5.2014	Dr. rer. nat.
Udvardi, Patrick	Pre- and postnatal effects of atomoxetine hydrochloride on maturing neurons in the rat brain	Prof. Dr. Ludolph, Andrea	Department of Adolescent Psychiatry and Psychotherapy	16.5.2014	Dr. rer. nat.
Dmochewitz, Lyda	Cellular uptake of clostridial C3 toxins and diphtheria toxin and the use of C3 toxins as protein delivery systems	Prof. Dr. Barth, Holger	Institute of Pharmacology and Toxicology	30.6.2014	Dr. rer. nat.
Palesch, David	Generation and characterization of AAV vectors for combination immunotherapy against HIV-1	Prof. Dr. Münch, Jan	Institute of Molecular Virology	23.7.2014	Dr. rer. nat.
Vogt, Julia	Mutational mechanisms underlying large NF1 deletions associated with neurofibromatosis type-1	Prof. Dr. Kehrer-Sawatzki, Hildegard	Institute of Human Genetics	12.9.2014	Dr. rer. nat.
Ireno, Ivanildce	Fluorescence based recombination assay for sensitive and specific detection of genotoxic carcinogens in human cells	Prof. Dr. Wiesmüller, Lisa	Department of Gynecology and Obstetrics	23.9.2014	PhD
Wehrle, Esther	Mechanostimulation of fracture healing by low-magnitude high-frequency vibration	Prof. Dr. Ignatius, Anita	Institute of Orthopedic Research and Biomechanics	24.10.2014	Dr. rer. nat.
Wu, Zeguang	Natural killer cells control human cytomegalovirus transmission in vitro and are effectors of the adaptive antiviral immunity	Prof. Dr. Mertens, Thomas	Institute of Virology	4.11.2014	PhD
Asam, Daniela	Identification of ß-haemolysin-encoding genes in Streptococcus anginosus	Prof. Dr. Spellerberg, Barbara	Institute of Medical Microbiology and Hygiene	24.11.2014	Dr. rer. nat.
Paul, Tanusree	Biomarkers for epidermal growth factor receptor inhibitor induced skin toxicity and drug response	Prof. Dr. Zolk, Oliver	Institute of Pharmacology of Natural Products and Clinical Pharmacology	3.12.2014	PhD
Thompson, Kristin	Localization and Function of P2X4 Receptors in the Respiratory Epithelium	Prof. Dr. Frick, Manfred	Institute of Applied Physiology	4.12.2014	PhD
Zhou, Yuan	Glucose substitution rescues lifespan of aging telomere dysfunctional mice by elevating glycolysis and IGF-1/mTOR dependent mitochondrial biogenesis	Prof. Dr. Rudolph, Karl Lenhard	Department of Molecular Medicine	16.12.2014	PhD
Obermeier, Kim	Functional classification of cells derived from patients carrying the Finnish PALB2 founder mutation	Prof. Dr. Wiesmüller, Lisa	Department of Gynecology and Obstetrics	7.1.2015	Dr. rer. nat.
Stöckle, Bettina	Synthesis of multivalent polymers for drug delivery and as surface coatings	Prof. Dr. Weil, Tanja	Institute of Organical Chemistry III	12.1.2015	Dr. rer. nat.
Wahler, Anke	Characterization of dimerization and nuclear signaling of engulfment adapter PTB domain containing 1 (GULP1)	Prof. Dr. von Arnim, Christine	Department of Neurology	11.2.2015	Dr. rer. nat.

Name	Topic	Main supervisor (names)	Institute	Date of final examination	Degree
Schneider, Vanessa	Investigation of immunogenic targets on leukemic stem cells in acute myeloid leukemia	Prof. Dr. Greiner, Jochen	Clinic for Internal Medicine II	12.2.2015	Dr. rer. nat.
Enlund, Eveliina	Role of MicroRNAs in the pathophysiology of obesity	Prof. Dr. Fischer-Posovszky, Pamela	Department of Pediatrics and Adolescent Medicine	13.2.2015	PhD
Assfalg, Robin	The nucleolus as a stress sensor	Prof. Dr. Iben, Sebastian	Institute of Dermatology and Allergic Disease	13.3.2015	Dr. rer. nat.
Koch, Sylvia	Cockayne syndrome protein A is a transcription factor of RNA polymerase I and stimulates ribosomal biogenesis and growth	Prof. Dr. Iben, Sebastian	Institute of Dermatology and Allergic Disease	13.3.2015	Dr. rer. nat.
Haffner-Luntzer, Melanie	Role of Midkine during fracture healing	Prof. Dr. Ignatius, Anita	Institute of Orthopedic Research and Biomechanics	20.3.2015	Dr. rer. nat.
Vogel Marion	FOXO1 partially restores the B-cell phenotype in classical Hodgkin lymphoma and induces features of plasma cell differentiation	Prof. Dr. Wirth, Thomas	Institute of Physiological Chemistry	31.3.2015	Dr. rer. nat.
Hering, Tanja	Brain, skeletal muscle and liver mitochondrial biology in the R6/2 fragment model of Huntington's Disease	PD Dr. Orth, Michael	Department of Neurology	29.6.2015	Dr. rer. nat.
Anastasiadou, Sofia	The role of Serum Response Factor mediated gene regulation in a mouse model of Multiple Sclerosis	Prof. Dr. Knöll, Bernd	Institute of Physiological Chemistry	30.7.2015	Dr. rer. nat.
Osswald, Annika	Tumor-targeting with anaerobic bacteria in three-dimensional tumor spheroids in vitro	Prof. Dr. Dürre, Peter	Institute of Microbiology and Biotechnology	6.8.2015	Dr. rer. nat.
Ernst, Katharina	The requirement of host cell chaperones and peptide-prolyl cis/trans isomerases for membrane translocation of bacterial ADP-ribosylating toxins in mammalian cells	Prof. Dr. Barth, Holger	Institute of Pharmacology and Toxicology	10.8.2015	Dr. rer. nat.
Cappadona, Ilaria	Regulation of human cytomegalovirus morphogenesis by the tegument protein complex pUL47/pUL48	Prof. Dr. Mertens, Thomas	Institute of Virology	26.8.2015	PhD
Kemmler, Julia	Oxygen treatment improves compromised fracture healing after thoracic trauma in mice	Prof. Dr. Ignatius, Anita	Institute of Orthopedic Research and Biomechanics	11.9.2015	Dr. rer. nat.
Bührdel, John	Analysis of Myofibrillar Myopathy related genes in zebrafish	Prof. Dr. Rottbauer, Wolfgang	Clinic for Internal Medicine II	14.9.2015	Dr. rer. nat.
Hempel, Annemarie	Characterization of Rcsd1 and Sox4 during Xenopus leaves organogenesis	Prof. Dr. Kühl, Michael	Institut für Biotechnologie und Molekulare Biologie	23.9.2015	Dr. rer. nat.
Mohr, Katharina	Establishment of an ELISA to detect the CXCR4 antagonist hSA(408-423) and characterization of CXCR4 mutants associated with WHIM syndrome	Prof. Dr. Münch, Jan	Institute of Virology	25.9.2015	Dr. rer. nat.
Fischer, Simon	Next-generation cell engineering of biopharmaceutical production cells using micro RNAs	Prof. Dr. Otte, Kerstin	Institute of Applied Biotechnology, Biberach	16.10.2015	Dr. rer. nat.
Kallert, Stephanie	Design and evaluation of strategies to optimize lipid specific T-cells responses against Mycobacterium tuberculosis	Prof. Dr. Stenger, Steffen	Institute of Medical Microbiology and Hygiene	27.10.2015	Dr. rer. nat.
Chhabra, Resham	Delivery of bioactive substances into the CNS using nanomedical approaches for the treatment of synaptopathies	Juniorprof. Dr. Grabrucker, Andreas	Institute for Anatomy and Cell Biology	3.11.2015	PhD

Name	Topic	Main supervisor (names)	Institute	Date of final examination	Degree
Qin, Ruifang	Mechanical force-dependent regulation of protein dynamics in focal adhesion	Prof. Dr. von Wiechert, Götz	Clinic for Internal Medicine I	18.12.2015	PhD
Kanwal, Noreen	Characterization of Spar3 in brain and lens development	Prof. Dr. Böckers, Tobias	Institute for Anatomoy and Cell Biology	21.12.2015	PhD
Duda, Johanna	Converging roles of altered Ca2+ homeostasis, impaired DNA-integrity and mitochondrial dysfunction for selective neuronal vulnerability	Prof. Dr. Liss, Birgit	Institute of General Physiology	23.11.2015	Dr. rer. nat.
Emmerling, Verena	Recombinant adeno-associated virus-based vectors for gene therapy: novel strategies towards improved manufacturing	Prof. Dr. Kochanek, Stefan	Department of Gene Therapy	18.1.2016	Dr. rer. nat.
Grieb, Melanie	Gene regulatory networks with a Boolean network extension incorporating uncertainty	Prof. Dr. Kestler, Hans	Institute for Medical Systems Biology	26.1.2016	Dr. rer. nat.
Zagotta, Ivana	The Effect of Resveratrol on Obesity Associated Fibrosis in Adipocytes	PD Dr. Fischer-Posovszky, Pamela	Department of Pediatrics and Adolescent Medicine	29.1.2016	PhD
Pasquarelli, Noemi	Pharmacological inhibition of monoacylglycerol lipase as a therapeutic strategy for neurodegenerative diseases	PD Dr. Witting, Anke	Department of Neurology	22.2.2016	Dr. rer. nat.
Meyer zu Reckendorf, Christopher	Identification and first functional characterization of general transcription factor TFII-I as a Serum Response Factor cofactor in neurons	Prof. Dr. Knöll, Bernd	Institute of Physiological Chemistry	11.3.2016	Dr. rer. nat.



Workshops	Date	Organizer
Gender Aspects/ Women in Science	12/09-12/10/2013	GRK 1789/1
German course – German for Beginners	every term, start 24/10/2013	IGradU
German course – German for Advanced Beginners	every second term, start 10/21/2013	IGradU
Job application training for doctoral students	02/21/2014	IGradU
Financial Planning for doctoral student	02/27/2014	IGradU
Good Scientific Practice	01/13/2014-01/14/2014	IGradU
Project Management for Research Projects – Advanced level	01/30/2014-01/31/2014	IGradU
Training on occupational dissability cover	06/26/2014	IGradU
Writing Theses and Papers in the Academic Context for experimental medicine	01/24/2014	IGradU
Writing Theses and Papers in the Academic Context	2.10.2014	IGradU
Data Analysis with R	03/06-03/07/2014	IGradU
Statistik Workshop	03/06-03/07/2014	GRK 1789/1
PhD/MD and then-Career Possibilities with a Start in Science!	03/17-03/18/2014	IGradU
Academic Writing	03/03/-03/04/2014	IGradU
Extramural Funding	05/05-05/06/2014	IGradU
Good Manufacturing Practice	5.12.2014	IGradU
Sicherheit in der Gentechnik	05/08-05/09/2014	IGradU
Statistics and Biological Data Analysis	every second Tuesday during term, start 04/22/2014	IGradU
FACS course	06/03/2014	GRK 1789/1
Project Management for Research Projects – Basic Level	06/04-06/05/2014	IGradU
Improved Reading	06/12/-06/13/2014	IGradU
Taxes seminar	03/07/2014	IGradU
Project Management in Biotech Industries	07/07/2014	IGradU
Biotech Quality Manager- Job insights and opportunities	07/08/2014	IGradU
Presentation Skills	07/17-07/18/2014	IGradU
Presentation and Charisma Coaching	09/04/2014	GRK 1789/1
Extramural Funding	11/03-11/04/2014	IGradU
FACS course	11/22/2014	IGradU, Medical Faculty
PhD/MD and then-Career Possibilities with a Start in Science!	12/01-12/02/2014	IGradU

Workshops	Date	Organizer
Writing Theses and Papers in the Academic Context	02/02/02/03/2015	IGradU
Improved Reading	02/26-02/27/2015	IGradU
Presentation Skills	03/05-03/06/2015	IGradU
Academic Writing	04/07-04/08/2015	IGradU
Good Manufacturing Practice	04/27/2015	IGradU
Extramural Funding	05/11-05/12/2015	IGradU
Sicherheit in der Gentechnik	05/21-05/22/2015	IGradU
Financial Planing for Doctoral Students	06/16/2015	IGradU
PhD/MD and then-Career Possibilities with a Start in Science!	06/29-06/30/2015	IGradU
Financial Education for Doctoral Students	07/03/2015	IGradU
vom Student zur Führungskraft und zum Unternehmer- Start-Up	07/14/2015	IGradU
Data Analysis with R	10/22-10/23/2015	IGradU
Extramural Funding	11/03-11/04/2015	IGradU
Project Management in Biotech Industries	11/09/2015	IGradU
Job Application Training for Doctoral Students	11/12/2015	IGradU
Financial Planing for Doctoral Students	11/19/2015	IGradU
Taxes seminar	11/26/2015	IGradU
PhD/MD and then-Career Possibilities with a Start in Science!	11/30-12/01/2015	IGradU
Writing Theses and Papers in the Academic Context	12/16/2015	IGradU
FACS course	01/22-01/23/2016	IGradU, Medical Faculty
Writing Theses and Papers in the Academic Context	02/01-02/02/2016	IGradU
FACS course	02/12-02/13/2016	IGradU, Medical Faculty
Good Scientific Practice	02/22-02/23/2016	IGradU

Excursions	Date	Organizer
TEVA/Ratiopharm Ulm	01/17/2014	IGradU
Roche Diagnostics GmbH	02/28/2014	IGradU
Boehringer Ingelheim Pharma GmbH & Co KG Biberach	04/03/2014	IGradU
Carl Zeiss AG	04/24/2014	IGradU
Amgen Research Penzberg	05/16/2014	IGradU
Roche Diagnostics GmbH	02/27/2015	IGradU
Boehringer Ingelheim Pharma GmbH & Co KG Biberach	03/12/2015	IGradU
Carl Zeiss AG	06/11/2015	IGradU
Roche Diagnostics GmbH	02/05/2016	IGradU

Symposia	Date	Organizer
Spring Meeting 2014	03/27-03/29/2014	IGradU
Fall Meeting 2014	10/09-10/11/2014	IGradU
Status Seminar on Immunmodulation	02/13/2015	BIU
3rd BIU Symposium	03/07/2015	BIU
Spring Meeting 2015	03/25-03/27/2015	IGradU
4th BIU Symposium	04/14/2015	BIU
Fall Meeting 2015	10/07/10/09/2015	IGradU

Summer and Winter Schools	Date	Organizer
8th Tongji-Ulm Summer School in Molecular Medicine: Cancer: From Molecules to Disease	07/28/-08/11/2014	IGradU
9th Tongji-Ulm Summer School in Molecular Medicine: Immunosupression and infectious complications	07/20/-08/01/2015	IGradU

Retreats	Date	Organizer
CEMMA Retreat, Autenried	04/04/-04/05/2014	GRK 1789/1
Joint Retreat Padua-Ulm within the joint PhD programme between the University of Padua and IGradU/Ulm University, Blaubeuren	07/11-07/13/2014	IGradU, Medical Faculty
Joint Retreat Oulu-Ulm within the joint PhD programme between Biocenter/Oulu and IGradU/Ulm University, Autenried	09/23-09/25/2014	IGradU, Biocenter Oulu
PhD-students retreat: "Advanced Concepts in Molecular Medicine", Lago di Como, Italy	05/04-05/06/2015	IGradU
Joint Retreat Oulu-Ulm within the joint PhD programme between Biocenter/Oulu and IGradU/Ulm University, Oulu, Finland	11/17-11/20/2015	Biocenter Oulu, IGradU

Social Activities	Date
Visit to the Musical "The Black Rider" at Theater Ulm	12/11/2015
Christmas Party	12/08/2015
Excursion to Nürnberg (including Christmas Market)	12/05/2015
Italian Evening	10/01/2015
Einstein Marathon 2015	09/27/2015
“Ulmer Kennenlerntag” (Guided Tour through Ulm, Boat Trip, Schwörkonzert Carmina Burana + Lichterserenade)	07/18/2015
Open-Air Concert of the Ulm Philharmonic Orchestra in the Glacis Park, Neu-Ulm	07/08/2015
Summer Party	07/01/2015
Excursion to Heidelberg	06/20/2015
Excursion to Münsingen /Schwäbische Alb (train trip)	02/27/2015
Excursion to Castle Neuschwanstein and the Christmas Market in Füssen	12/13/2014
Farewell Meeting for the M4M Coordinator Nicola Haff	12/10/2014
Christmas Party	12/02/2014
Visit to the Main Mosque in Ulm	11/08/2014
Guided Tour of the Ulmer Münster	10/18/2014
Visit to the Octoberfest 2014	10/02/2014
Einstein Marathon 2014	09/28/2014
Visit to the French Village (Friedrichsau)	08/29/2014
Excursion to Ludwigsburg Residential Palace	08/23/2014
Visit to a Jazz Concert at Glacis Park, Neu-Ulm	07/29/2014
Summer Party	07/03/2014
Visit to the Ulm International Festival and Culture Parade	06/28/2014
Seminar Intercultural Training	06/13/2014
Meeting at the Danube Office	05/13/2014
Excursion to the Limes Museum Aalen	04/12/2014
Visit to the Exhibition “Impressive Moments Abroad”	04/12/2014
Bowling	03/05/2014
Excursion to the Ulmer Museum	01/09/2014
Excursion to Esslingen (including Christmas Market)	12/07/2013
Christmas Party	02/12/2013
Legal advice	11/30/2013
Excursion to the Minnesängersaal at the Reichenauer Hof, Ulm	11/28/2013
Visit of the Botanical Gardens and Autumn Festival	10/14/2013

Invited Speakers (2013-2015)

Topic	Speaker	Date	Organizer
Enzymatic regulation of the synthesis of collagens, the major protein class of extracellular matrix	Johanna Myllyharju Oulu/Finland	12/02/2015	IGradU
Enzymatic regulation of hypoxia response as a therapeutic target	Johanna Myllyharju Oulu/Finland	11/30/2015	IGradU
Hypoxia response pathway - a molecular survival mechanism under reduced tissue oxygenation	Johanna Myllyharju Oulu/Finland	11/25/2015	IGradU
Multiple contributions of homologous recombination factors to the replication of UV damaged DANN	Vanesa Gottifredi Buenos Aires/Argentina	11/03/2015	IGradU
Is the fidelity of DNA replication a fact or a myth?	Vanesa Gottifredi Buenos Aires/Argentina	11/02/2015	IGradU
Cortactin controls adherens junction assembly	Florian Heidel Magdeburg/Germany	10/09/2015	IGradU
Zebrafish through the looking glass: an in vivo glimpse at cardiovascular development and pathophysiology	Salim Seyfried Potsdam/Germany	10/09/2015	IGradU
Whole exome sequencing reveals tandem-of-two-pore “leak channels” as novel arrhythmia genes	Niels Decher Marburg/Germany	10/09/2015	IGradU
TDP-43 repression of non-conserved cryptic exons is compromised in ALS-FTD	Philip Wong Baltimore/USA	10/08/2015	IGradU
Telomerase sensitizes mammalian cells to aneuploidy-induced transformation by alleviating telomere replication stress	Cagatay Günes Jena/Germany	10/08/2015	IGradU
Targeting LRH1/NR5A2 to treat Type 1 Diabetes Mellitus	Benoit Gauthier Sevilla/Germany	10/08/2015	IGradU
Multifaceted dysfunctions caused by polyglutamine expansion in neurodegenerative disorders	Yvon Trottier Illkirch/France	10/08/2015	IGradU
Epigenetic and chromosoms	Heinrich Leonhardt Munich/Germany	10/07/2015	IGradU
Cytomegalovirus latency – staying alive during latent infection	John Sinclair Cambridge/UK	06/10/2015	IGradU
Translating a basic knowledge of herpesvirus infection into a novel therapy for Parkinson’s disease	John Sinclair Cambridge/UK	06/09/2015	IGradU
Epigenetic regulation of human cytomegalovirus lytic and latent infection	John Sinclair Cambridge/UK	06/08/2015	IGradU
Targeted editing of the human (Epi)genome for therapeutic applications	Angelo Lombardo Milano/Italy	05/05/2015	IGradU
Combining computational chemistry and biochemistry as a tool in rational drug design	Giorgio Cozza Padua/Italy	05/05/2015	IGradU

Topic	Speaker	Date	Organizer
Analyzing structures with the PyMOL software	Rhett A. Kovall Cincinnati/USA	05/26/2015	IGradU
Structure and function of the CSL-SPEN Corepressor Complex — a negative regulator of notch signaling	Rhett A. Kovall Cincinnati/USA	05/21/2015	IGradU
The structual biology of notch signaling	Rhett A. Kovall Cincinnati/USA	06/20/2015	IGradU
Analysing the secretome of pancreatic cancer cells by affinity proteomics	Jörg Hoheisel Heidelberg/Germany	03/27/2015	IGradU
NFATc1 transcription factor in pancreatic cancer development and progression	Volker Ellenrieder Göttingen/Germany	03/27/2015	IGradU
NF-kappa B in the nervous system	Christian Kaltschmidt Bielefeld/Germany	03/27/2015	IGradU
Crucial roles of collagen XIII in neuromuscular junction regeneration and functional recovery following peripheral nerve injury	Zarin Zainul Oulu/Finland	03/27/2015	IGradU
Stem cells and neurodegeneration: from disease modeling to drug discovery	Jared Sterneckert Dresden/Germany	03/27/2015	IGradU
Patterned thermoplasmonic gold nanostructures for sub-cellular manipulation	Julien Polleux Munich/Germany	03/26/2015	IGradU
A genetic mechanism for tibetan high-altitude adaptation	Mikko Myllymäki Oulu/Finland	03/26/2015	IGradU
Mitochondrial activity determines hematopoietic stem cell fate decisions	Matthias Lütolf Lausanne/Switzerland	03/26/2015	IGradU
Body building: molecular and evolutionary mechanisms in planarian regeneration	Jochen Rink Dresden/Germany	03/26/2015	IGradU
Dynamics of DNA methylation during cardiomyocyte development and disease	Lutz Hein Freiburg/Germany	03/26/2015	IGradU
Stem cells in fish. Permanent growth and constant decisions	Lázaro Centanin Heidelberg/Germany	03/25/2015	IGradU
Two highlight papers: resident versus recruited macrophages in tissue homeostasis	Bénédicte Chazaud Lyon/France	02/25/2015	IGradU
Inflammation in tissue repair	Bénédicte Chazaud Lyon/France	02/24/2015	IGradU
Engineering and maturing human heart muscle	Wolfram-Hubertus Zimmermann Göttingen/ Germany	02/10/2015	IGradU

Topic	Speaker	Date	Organizer
Streptococcus gallolyticus: a commensal bacterium associated with colon cancer	Shaynoor Dramsi Paris/France	01/19/2015	IGradU
From RNAi phenotype to molecular antagonists: development of E3-ligase inhibitors of IDOL	Jörg Rippmann Biberach/Germany	10/11/2014	IGradU
Epigenetics in lymphoma – Role of PRC2	Thomas Berg Frankfurt/Germany	10/11/2014	IGradU
Helper-dependent adenoviral vectors; applications in gene and cell therapy	Philip Ng Houston/USA	10/10/2014	IGradU
Progress of EBNA1/oriP-based vectors and its derivatives in gene therapy	Aloys Schepers Munich/Germany	10/10/2014	IGradU
Contribution of peripheral innate response to neurodegeneration	Ana Martin-Villalba Heidelberg/Germany	10/10/2014	IGradU
Mutant SOD1-toxicity in ALS: from soluble proteins to aggregate formation	Albrecht m. Clement Mainz/Germany	10/10/2014	IGradU
Mitochondrial shaping proteins and the control of protein synthesis and degradation	Marco Sandri Padua/Italy	10/10/2014	IGradU
The wilms tumor protein Wt1 acts in different places: from the kidney to the CN	Christoph Englert Jena/Germany	10/10/2014	IGradU
The contribution of neuroinflammation in motoneuron disorders	Cedric Raoul Montpellier/France	10/10/2014	IGradU
Targeting neuroprotective strategies in Huntington's disease	Flaviano Giorgini Leicester/UK	10/10/2014	IGradU
Alzheimer's disease: lessons from animal models	Philip Wong Baltimore/USA	10/09/2014	IGradU
Mapping genes underlying dynamic disease traits using molecular markers: examples from animal and plant data	Mikko Sillanpää Oulu/Finland	09/25/2014	IGradU
Effects of collagen XVIII on adipogenesis and metabolism	Tanja Pihlajaniemi Oulu/Finland	09/25/2014	IGradU
Targeting mechanisms of cell & tissue interactions behind organogenesis	Seppo Vainio Oulu/Finland	09/25/2014	IGradU
In silico modeling and simulation of proteins and membranes	André Juffer Oulu/Finland	09/25/2014	IGradU
HIF prolyl 4-hydroxylases as therapeutic target	Johanna Myllyharju Oulu/Finland	09/24/2014	IGradU
Glycogen synthase kinase-3 regulates degradation of hypoxia-inducible factor-1alpha	Thomas Kietzmann Oulu/Finland	09/24/2014	IGradU

Topic	Speaker	Date	Organizer
MnSOD (SOD2) opposes tumorigenesis in hepatocytes	Anja Konzack Oulu/Finland	09/24/2014	IGradU
The role of Wnt5a in kidney morphogenesis	Susanna Kaisto Oulu/Finland	09/24/2014	IGradU
Solute traffic across peroxisomal membrane – a question of life or death	Kalervo Hiltunen Oulu/Finland	09/24/2014	IGradU
Seeing is believing – dissecting signal transduction through microscopy	Christian Bökel Dresden/Germany	09/22/2014	IGradU
Reactive oxygen species as mediators for the metabolic zonation in the liver	Thomas Kietzmann Oulu/Finland	07/29/2014	IGradU
Oxygen sensing: old features – new aspects	Thomas Kietzmann Oulu/Finland	07/28/2014	IGradU
Muscle homeostasis and the extracellular matrix	Sibilla Molon Padua/Italy	07/12/2014	IGradU
Mechanotransduction	Tito Panciera Padua/Italy	07/12/2014	IGradU
Autophagy in muscledisease	Paolo Grumati Padua/Italy	07/12/2014	IGradU
The role of increased O2 tensions in hemorrhagic shock	Chiara Volani Padua/Italy	07/12/2014	IGradU
Biophysical analysis of connexin-32 channel function and dysfunction in the peripheral nervous system	Mario Bortolozzi Padua/Italy	07/12/2014	IGradU
Role of cellular proteins in thel ate steps of lentiviral replication	Michele Celestino Padua/Italy	07/12/2014	IGradU
Development of new influenza drugs	Beatrice Mercorelli Padua/Italy	07/12/2014	IGradU
Wnt and Hippo signaling: two sides of the same coin	Luca Azzolin Padua/Italy	07/12/2014	IGradU
Vaccination against the HER-2/neu with a new polymer-based vaccine	Debora Carpanese Padua/Italy	07/12/2014	IGradU
Initiation and transmission of AA-amyloidosis	Per Westermark Uppsala/Sweden	06/30/2014	IGradU
A bone to pick with zebrafish – genetic analysis of osteogenesis	Stefan Schulte-Merker Utrecht/Netherlands	06/16/2014	IGradU
Systemic onset juvenile arthritis: an autoinflammatory disease	Elizabeth Mellins Stanford/USA	06/04/2014	IGradU

Topic	Speaker	Date	Organizer
MHC class II antigen presentation: why are certain allels risk factors for disease?	Elizabeth Mellins Stanford/USA	06/02/2014	IGradU
Class II antigen presentation: new insights into the pathway	Elizabeth Mellins Stanford/USA	05/28/2014	IGradU
Mechanisms of post-translational control of gene expression in response to cell stress	Dieter Wolf Stanford/USA	05/28/2014	SFB 1074
Global approaches to identifying new drug targets in prostate cancer	Dieter Wolf Stanford/USA	05/27/2014	IGradU
Identification and validation of a therapeutic target for ALS-FTD	Philip Wong Baltimore/USA	05/26/2014	IGradU
From axis formation to heart development: lessons from zebrafish	Jeroen Bakkers Utrecht/Netherlands	05/26/2014	IGradU
Raft protein clustering regulates Ras signaling via isoform-dependent depalmitoylation and membrane interactions	Yoav I. Henis Tel Aviv/Israel	04/25/2014	IGradU
The role of stress activated signaling pathways in acute myeloid leukemia	Stephen M. Sykes Philadelphia/USA	03/29/2014	IGradU
Identifying therapeutic targets in AML using functional genomics	Stefan Fröhling Heidelberg/Germany	03/29/2014	IGradU
Reconstitution of proteins into lipid bilayers: general principles and application to a difficult case: the light-harvesting 1 complex from Rhodospirillum rubrum	Rogin Ghosh Stuttgart/Germany	03/28/2014	IGradU
Novel approaches for synthesis and characterization of membrane proteins	Christoph Zaba Vienna/Austria	03/28/2014	IGradU
DNA replication and cancer	Helmut Pospiech Oulu/Finland	03/28/2014	IGradU
Epigeneticcontrolofaxonal regeneration	Simone di Giovanni London/UK	03/28/2014	IGradU
Dysregulated SRF triggers formation of hepatocellular carcinoma	Alfred Nordheim Tübingen/Germany	03/28/2014	IGradU
GPCRs in development and disease	Marc Caron Durham/USA	03/27/2014	IGradU
Relevance of animal models for multiple sclerosis research	Martin Stangel Hannover/Germany	02/27/2014	IGradU
Composition and function of the TBX5 and TBX20 cardiac interactome	Frank Colon Chapel Hill/USA	02/26/2014	IGradU
Basic principles underlying ion channel function: a biochemical and structural perspective	Eduardo Perozo Chicago/USA	01/23/2014	IGradU

Topic	Speaker	Date	Organizer
Structural basis of voltage-sensing in ion channels and enzymes	Eduardo Perozo Chicago/USA	01/22/2014	IGradU
Challenges in ex vivo investigation of lung fluid homeostasis	Robert Tarran Chapel Hill/USA	12/06/2013	IGradU
From bench to bedside: translational research in chronic lung disease	Robert Tarran Chapel Hill/USA	12/05/2013	IGradU
Who phosphorylates secreted proteins? An unanticipated answer to a vexed question	Lorenzo Pinna Padua/Italy	11/14/2013	IGradU
CK2: an atypical member of the oncokinome	Lorenzo Pinna Padua/Italy	11/13/2013	IGradU
Who phosphorylates whom? The messy issue of kinases specificity	Lorenzo Pinna Padua/Italy	11/12/2013	IGradU
Ras chaperons for cancer therapy-beginning of randomized phase II in NSLC	Yoel Kloog Tel Aviv/Israel	10/12/2013	IGradU
On the role of chronic hepatitis in driving liver cancer of different aetiologies	Mathias Heikenwälder Munich/Germany	10/12/2013	IGradU
Models to understand Myc function in human tumors	Martin Eilers Würzburg/Germany	10/12/2013	IGradU
Weibel-Palade Bodies: endothelial organelles providing first aid to the vasculature	Daniel Cutler London/UK	10/11/2013	IGradU
Scaffold proteins and signal transduction: implications for disease and therapeutic intervention	Lukas Huber Innsbruck/Austria	10/11/2013	IGradU
Self-repairing broken hearts	Anna Jazwinska Fribourg/Switzerland	10/11/2013	IGradU
Ligand oligomerization state controls Tie2 receptor trafficking and angiopoietin-2-specific responses	Riikka Pietilö Oulu/Finland	10/11/2013	IGradU
Venous malformation causing mutations have different effects on endothelial Tie2 receptor	Marjut Nätynki Oulu/Finland	10/11/2013	IGradU
What the embryo can tell us about NSCs: a tale of two stem cells	Sally Moody Washington D.C./USA	10/11/2013	IGradU
Heart regeneration: what is the difference between zebrafish and mammals	Michael Engel Erlangen/Germany	10/09/2013	IGradU

Publications of PhD students and Junior Faculty 2013-2016

(as of February 2016, Doctoral Students are marked in blue)

2013

Neu C, Sedlag A, **Bayer C**, Förster S, Crauwels P, Niess JH, van Zandbergen G, Frascaroli G, Riedel CU (2013): CD14-dependent monocyte isolation enhances phagocytosis of listeria monocytogenes by proinflammatory, GM-CSF-derived macrophages. PLoS One. 2013 Jun 11;8(6):e66898.

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 (2013): PGC-1α is a male-specific disease modifier of human and experimental amyotrophic lateral sclerosis, Hum Mol Genet

Bischof J1, Randoll SJ, Süßner N, Henne-Bruns D, Pinna LA, Knippschild U (2013): CK1δ kinase activity is modulated by Chk1-mediated phosphorylation. PLoS One. 2013 Jul 4;8(7):e68803.

Atherton J, Kurbatskaya K, Bondulich M, Croft C L, Garwood C J, **Chhabra R**, Wray S, Jeromin A, Hanger DP, Noble W (2013): Calpain cleavage and inactivation of the sodium calcium exchanger-3 occur downstream of Aβ in Alzheimer's disease. Aging Cell 2013; 13(1): 49–59.

Miklavc P, **Ehinger K**, **Thompson KE**, Hobi N, Shimshek DR, Frick M. (2013): Surfactant Secretion in LRRK2 Knock-Out Rats: Changes in Lamellar Body Morphology and Rate of Exocytosis. PLOS ONE

Fan C1, Lehmann-Horn F, Weber MA, **Bednarz M**, Groome JR, Jonsson MK, Jurkat-Rott K (2013): Transient compartment-like syndrome and normokalaemic periodic paralysis due to a Ca(v)1.1 mutation. Brain. 2013 Dec;136(Pt 12):3775-86.

Fischer S, Wagner A, Kos A, Aschrafi A, Handrick R, Hannemann J, Otte K (2013): Breaking limitations of complex culture media: functional non-viral miRNA delivery into pharmaceutical production cell lines. J Biotechnol 168(4):589-600.

Führer M, Pannicke U, Schuetz C, Jacobsen EM, Schulz A, Friedrich W, Schwarz K, Hoenig M (2013) Successful Haploidentical Hematopoietic Stem Cell Transplantation in a Patient with SCID Due to CD3ε Deficiency: Need for IgG-Substitution 6 Years Later. Klin Padiatr

Grabrucker S, Jannetti L, Eckert M, Gaub S, **Chhabra R**, **Pfaender S**, Mangus K, Reddy PP, Rankovic V, **Schmeisser MJ**, Kreutz MR, Ehret G, Boeckers TM, **Grabrucker AM** (2013): Zn2+ deficiency dysregulates the synaptic ProSAP/Shank scaffold and might contribute to autism spectrum disorders. Brain 2013; 137 (1): 137-52.

Guo Y, et al. (2013): Comparative analysis reveals distinct and overlapping functions of mef2c and mef2d during cardiogenesis in Xenopus laevis. Plos One 2013

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. J Orthop Res. 2013 Nov;31(11):1845-50.

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. 2013 Dec 31;8(12):e84232.

Sprinzl MF, Reisinger F, Puschnik A, Ackermann K, **Hartmann D**, Schiemann M, Weinmann A, Galle PR, Schuchmann M, Otto G, Friess H, Heikenwälder M, Protzer U (2013): Sorafenib perpetuates cellular anti-cancer effector functions by modulating the cross talk between macrophages and natural killer cells. Hepatology.

Beitzinger C*, **Bronnhuber A***, Duscha K, Riedl Z, Huber-Lang M, Benz R, Hajós G, Barth H (2013): Designed azolopyridinium salts block protective antigen pores in vitro and protect cells from anthrax toxin. PLoS One. 2013 Jun 20;8(6):e66099; *contributed equally

Hermann M, Maier F, Masroor A, **Hirth S**, Pfitzner AJ, Pfitzner UM (2015): The Arabidopsis NIMIN proteins affect NPR1 differentially. Front Plant Sci. 2013 Apr 12;4:88

Kumar M, Witt B, Knippschild U, **Koch S**, **Meena JK**, Heinlein C, et al. (2013): CEBP factors regulate telomerase reverse transcriptase promoter activity in whey acidic protein-T mice during mammary carcinogenesis. International Journal of Cancer. 2013;132(9):2032-43.

Loos C, Syrovets T, Musyanovych A, Mailänder V, Landfester K, Simmet T (2013): Amino-functionalized nanoparticles as inhibitors of mTOR and inducers of cell cycle arrest in leukemia cells. Biomaterials. 2014 Feb;35(6):1944-53. doi: 10.1016/j.biomaterials.2013.11.056.

Palesch D and Kirchhoff F (2013): First Steps toward a Globally Effective HIV/AIDS Vaccine. Cell 155, 495_497.

Stürzel CM*, **Palesch D***, Khalid M*, Wissing S, Fischer N, and Münch J (2013): Utilization of Replication-Competent XMRV Reporter-Viruses Reveals Severe Viral Restriction in Primary Human Cells. PloS One 8, e74427.

Palesch D, Varga E, Marx UC, Vitzithum K, Kreutzmann P, Forssmann W, Münch J, Mägert H (2013): Domain 15 of the serine proteinase inhibitor LEKTI blocks HIV infection in vitro. Med J Indones, 22:131-5.

Parmar S, Schumann C, Ruediger S, Boeck S, Heinemann V, Kächele V, Seeringer A, **Paul T**, Seufferlein T and Stingl JC (2013): Pharmacogenetic predictors for EGFR-inhibitor- associated skin toxicity. The Pharmacogenomics Journal 13: 181_188 (2013).

Qi Y, Jiang D, Sindrilaru A, Treiber N, Rojewski M, Schrezenmeier H, Stegemann A, Vander Beken S, Schatz S, Wlaschek M, Böhm M and Scharffetter-Kochanek K (2013): TSG-6 Released From Mesenchymal Stem Cells Accelerates Wound Healing and Reduces Scar Formation in Murine Full-Thickness Skin Wounds. J Invest Dermatol. 2014 Feb;134(2):526-37. doi: 10.1038/jid.2013.328.

Jiang D*, **Qi Y***, Walker GN, Sindrilaru A, Hainzl A, Wlaschek M, MacNeil S, and Scharffetter-Kochanek K (2013): Adipose tissue derived mesenchymal stem cells delivered by a chemically defined carrier accelerate mouse acute cutaneous wound healing. Biomaterials. 2013,34(10):2501-2515. *contributed equally

Richter J, **Bischof J**, Zaja M, et al. (2013): Difluoro-dioxolo-benzoimidazol-benzamides as potent inhibitors of CK1δ and ε with nanomolar inhibitory activity on cancer cell proliferation. J Med Chem 2014, 57(19), 7933-7946.

Rossini V, Radulovic K and Niess JH (2013): Pathophysiologie und Therapie chronisch entzündlicher Darmerkrankungen. Verdauungskrankheiten, Vol. 31, Nr. 1/2013, S. 3-10.

Radulovic K, **Rossini V**, Manta C, Holzmann K, Kestler HA and Niess JH (2013): The Early Activation Marker CD69 Regulates the Expression of Chemokines and CD4 T Cell Accumulation in Intestine. Plos One 2013 Jun 12;8 (6): e65413.

Rossini V, Zhurina D, Radulovic K, Manta C, Leithauser F, Riedel CU and Niess JH (2013): CX3CR1+ Phagocytes Support the Activation of CD4 T Cells in an Antigen-Driven Colitis Model.Mucosal Immunol. 2014 May;7(3):533-48. doi: 10.1038/mi.2013.70.

Schneider C, Grois J, Renz C, Gronemeyer T, Johnsson N (2013) Septin rings act as template for myosin higher-order structures and inhibit redundant polarity establishment (2013) J Cell Sci. 2013 Aug 1;126(Pt 15):3390-400.

Greiner J, **Schneider V**, Schmitt M, Götz M, Döhner K, Wiesneth M, Döhner H, Hofmann S (2013): Immune responses against the mutated region of cytoplasmatic NPM1 might contribute to the favorable clinical outcome of AML patients with NPM1 mutations (NPM1mut). Blood. 2013 Aug 8 (IP 9.775).

Schneider V, Egenrieder S, Götz M, Herbst C, Greiner J, Hofmann S (2013): Specific immune responses against epitopes derived from Aurora kinase A and B in acute myeloid leukemia. Leuk Lymphoma. 2013 Jul;(IP 2.605).

Singh K, Gatzka M, Peters T, Borkner L, Hainzl A, Wang H, Sindrilaru A, Scharffetter-Kochanek K (2013): Reduced CD18 levels drive Treg conversion into Th17 cells in the CD18hypo PL/J mouse model of psoriasis. J Immunol. 190:2544-53.

Steinestel K, Gläsle F, Brüderlein S, Steinestel J, Pröpper C, Möller P (2013): Abelson interactor 1 (Abi1) in colorectal carcinoma: from synaptic plasticity to tumor cell migration. Pathologe. 2013 Nov;34 Suppl 2:189-94.

Maier M, Kraft K, **Steinestel K**, Schramm A, Lorenz KJ, Tisch M, Schwerer M, Maier H (2013): Human papillomavirus in squamous cell cancer of the head and neck: A study at the Ulm Military Hospital, Germany. HNO 2013; 61(7):593-601.

Steinestel K, Geiger A, Naraghi R, Kunz U, Danz B, Kraft K, Freude G (2013): Fatal thromboembolism to the left pulmonary artery by locally applied hemostatic matrix after surgical removal of spinal schwannoma: a case report. Human Pathology 2013; 44(2):294-8.

Stiefel et al. (2013): „ Identificationof process relevant miRNA in CHO cell lines - Process profiling reveals interesting targets for cell line engineering.“ BMCProceedings 2013 7 (Suppl6):P81.

Miklavc P, **Thompson KE** and Frick M (2013): A new role for P2X4 receptors as modulators of lung surfactant secretion. Front. Cell. Neurosci. 7:171.

Thompson KE, Korbmacher JP, Hecht E, Hobi N, Wittekindt OH, Dietl P, Kranz C, Frick M. FASEB J (2013): Fusion-activated Cation Entry (FACE) via P2X4 Couples Surfactant Secretion and Alveolar Fluid Transport. 2013 Apr;27(4):1772-83

Sears PR, **Thompson K**, Knowles MR, Davis CW (2013): Am J Physiology Lung Cell Molecular Physiology. Human Airway Ciliary Dynamics. 2013 Feb 1; 304(3):L170-83.

Udvardi PT, Foehr K, Henes C, Liebau S, Dreyhaupt J, Boeckers TM, Ludolph AG (2013): Atomoxetine affects transcription/translation of NMDA receptor and the norepinephrine transporter in the rat brain - an in vivo study. Drug Des Devel Ther. 2013 Dec 4;7:1433-46. doi: 10.2147/DDDT.S50448.

Udvardi PT, **Nespoli E**, **Rizzo F**, Hengerer B, Ludolph AG (2013): Nondopaminergic Neurotransmission in the Pathophysiology of Tourette Syndrome. International Review of Neurobiology, Chapter 4, 94-121 Int Rev Neurobiol.

Bengesser K, **Vogt J**, Mussotter T, Mautner VF, Messiaen L, Cooper DN, Kehrer-Sawatzki H (2013): Analysis of crossover breakpoints yields new insights into the nature of the gene conversion events associated with large NF1 deletions mediated by nonallelic homologous recombination. Hum Mutat. 2014 Feb; 35(2):215-26.

Wahler A, **Beyer AS**, Keller IE, Schnack C, **von Einem B**, Pröpper C, Boeckers TM, Peltan ID, Strickland DK, Hyman BT, von Arnim CA (2013): Engulfment adapter phosphotyrosine-binding-domain-containing 1 (GULP1) is a nucleocytoplasmic shuttling protein and is transactivationally active together with low-density lipoprotein receptor-related protein 1 (LRP1). Biochem J. 2013.

Recknagel S, Bindl R, Goeckelmann M, **Wehrle E**, Gebhard F, Huber-Lang M, Claes L & Ignatius A (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(3): 465-71.

Zagotta I, Dimova EY, **Funcke JB**, Wabitsch M, Kietzmann T, 2 , and Fischer-Posovszky P 1. (2013): Resveratrol Suppresses PAI-1 Gene Expression in a Human In Vitro Model of Inflamed Adipose Tissue. Oxid Med Cell Longev. 2013; 2013: 793525.

2014

Asam D & Spellerberg B (2014): Molecular pathogenicity of Streptococcus anginosus. Molecular oral microbiology.

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. Nature Communications (2014) 5, Article number: 4599

Böck C, Karabatsiakis A, Kolassa I-T (2014): Biologische Grundlagen der Depression – Mitochondriale Funktionalität als Ansatzpunkt. Zeitschrift für Medizin-Ethik-Recht.

Böck C*, Karabatsiakis A*, Manrique JS, Kolassa S, Calzia E, Dietrich DE, Kolassa I-T (2014): Mitochondrial respiration in peripheral blood mononuclear cells correlates with depressive subsymptoms and severity of major depression. Translational Psychiatry, 4, e397. * Co-first authors.

Tosi G1, Vilella A2, **Chhabra R3**, **Schmeisser MJ4**, Boeckers TM4, Ruozi B1, Vandelli MA1, Forni F1, Zoli M2, **Grabrucker AM5** (2014): Insight on the fate of CNS-targeted nanoparticles. Part II: Intercellular neuronal cell-to-cell transport. J Control Release. 2014 Mar 10;177:96-107.

Chhabra R1, **Grabrucker AM2**, Veratti P3, Belletti D3, Boeckers TM4, Vandelli MA3, Forni F3, Tosi G3, Ruozi B5 (2014): Characterization of lysosome-destabilizing DOPE/PLGA nanoparticles designed for cytoplasmic drug release. Int J Pharm. 2014 Aug 25;471(1-2):349-57.

Mühling T*, **Duda J*,** Weishaupt J, Ludolph AC and Liss B (2014): Elevated mRNA-levels of distinct mitochondrial and plasma membrane Ca2+ transporters in individual hypoglossal motor neurons of endstage SOD1 transgenic mice. Front Cell Neurosci. Nov 14;8:353.

Xu J, Chai H*, **Ehinger K***, Egan TM, Srinivasan R, Frick M and Khakh BS (2014): Imaging P2X4 receptor subcellular distribution, trafficking, and regulation using P2X4-pHluorin. J. Gen. Physiol. 144:81–104. doi:10.1085/jgp.201411169. * these authors contributed equally to this work

Miklavc P*, **Ehinger K***, **Thompson KE**, Hobi N, Shimshek DR and Frick M (2014): Surfactant secretion in LRRK2 knock-out rats: changes in lamellar body morphology and rate of exocytosis. PLoS One. 9:e84926.

Enlund E, **Fischer S**, Handrick R, Otte K, Debatin KM, Wabitsch M, Fischer-Posovszky P (2014): Establishment of Lipofection for Studying miRNA Function in Human Adipocytes. PLoS One. 2014 May 21;9(5):e98023.

Fischer S, Buck T, Wagner A, Ehrhart C, Giancaterino J, Mang S, Schad M, Mathias S, Aschrafi A, Handrick R and Otte K (2014): A functional high-content miRNA screen identifies miR-30 family to boost recombinant protein production in CHO cells. Biotechnol J 9(10):1279-92.

Kumar S T, Meinhardt J, **Fuchs A-K**, Aumüller T, Leppert J, Büchele B, Knüpfer U, Ramachandran R, Yadav J K, Prell,E, et al. (2014): Structure and Biomedical Applications of Amyloid Oligomer Nanoparticles. ACS Nano 2014, 8, 11042–11052.

Xie L, Ritz O, Leithäuser F, Guan H, Färbinger J, Weitzer CD, **Gehringer F**, Bruederlein S, Holzmann K, **Vogel MJ**, Möller P, Wirth T, Ushmorov A (2014): FOXO1 downregulation contributes to the oncogenic program of primary mediastinal B-cell lymphoma. Oncotarget 5: 5392-5402.

Grabrucker S1, Pröpper C2, Mangus K3, **Eckert M3**, **Chhabra R3**, **Schmeisser MJ2**, Boeckers TM2, **Grabrucker AM4** (2014): The PSD protein ProSAP2/Shank3 displays synapto-nuclear shuttling which is deregulated in a schizophrenia-associated mutation. Exp Neurol 2014; 253: 126-37.

Grozdanov V, **Bliederhaeuser C**, Ruf WP, Roth V, Fundel-Clemens K, **Zondler L**, Brenner D, Martin-Villalba A, Hengerer B, Kassubek J, Ludolph AC, Weishaupt JH, **Danzer KM** (2014): Inflammatory dysregulation of blood monocytes in Parkinson's disease patients. Acta Neuropathol. 2014 Nov;128(5):651-63.

Haffner-Luntzer M, Heilmann A, Rapp A, Beie S, Schinke T, Amling M, Ignatius A, Liedert A (2014): Midkine-deficiency delays chondrogenesis during the early phase of fracture healing in mice. PLoS One. PLoS One. 2014 Dec 31;9(12):e116282.

Bronnhuber A, Maier E, Riedl Z, Hajós G, Benz R, Barth H (2014): Inhibitions of the translocation pore of Clostridium botulinum C2 toxin by tailored azolopyridinium salts protects human cells from intoxication. Toxicology. 2014 Feb 28;316:25-33.

Pylatiuk C, Sanchez D, Mikut R, Alshut R, Reischl M, **Hirth S**, Rottbauer W, Just S (2014): Automatic zebrafish heartbeat detection and analysis for zebrafish embryos. Zebrafish. 2014 Aug;11(4):379-83.

Ireno IC, Baumann C, Stöber R,Hengstler JG, Wiesmüller L (2014): Fluorescence based recombination assay for sensitive and specific detection of genotoxic carcinogens in human cells. Archives of Toxicology 88(5): 1141-1159.

Gole B1, Baumann C1, Mian E1, **Ireno IC1**, Wiesmüller L (2014): Endonuclease G initiates DNA rearrangements at the MLL breakpoint cluster upon replication stress. . Oncogene. 2015 Jun;34(26):3391-401.

Ireno IC1, **Wiehe RS1**, Stahl AI2, **Hampp S2**, Aydin S3, Troester MA4, Selivanova G5, Wiesmüller L1 (2014): Modulation of the poly (ADP-ribose) polymerase inhibitor response and DNA recombination in breast cancer cells by drugs affecting endogenous wild-type p53. Carcinogenesis. 2014 Oct;35(10):2273-82.

McCook O, Radermacher P, Volani C, Asfar P, Ignatius A, **Kemmler J**, Moeller P, Szabo C, Whiteman M, Wood ME, Wang R, Georgieff M, Wachter U (2014): H2S during circulatory shock: some unresolved questions. Nitric Oxide. 2014 Sep 15; 41:48-61.

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. 2014;13(13):2029-37.

Knippschild U, **Krueger M, Richter J**, Xu P, García-Reyes B, Peifer C, Halekotte J, Bakulev V, Bischof J (2014): The CK1 family: contribution to cellular stress response and its role in carcinogenesis. Front Oncol 2014;4(96)

Mack K, Kluge SF, Iyer SS, Pujol FM, Heigele A, Learn GH, Usmani SM, Sauter D, **Joas S**, **Hotter D**, Bibollet-Ruche F, Plenderleith LJ, Peeters M, Geyer M, Sharp PM, Fackler OT, Hahn BH, Kirchhoff F (2014): Nef proteins of epidemic HIV-1 group O strains antagonize human tetherin. Cell Host Microbe. 2014 Nov 12;16(5):639-50.

Müller K, Andersen PM, Hübers A, **Marroquin N**, Volk AE, **Danzer KM**, Meitinger T, Ludolph AC, Strom TM, Weishaupt JH (2014): Two novel mutations in conserved codons indicate that CHCHD10 is a gene associated with motor neuron disease. Brain 2014 Dec; 137(Pt 12): e30

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** (2014): Polymerase chain reaction and Southern blot-based analysis of the C9orf72 hexanucleotide repeat in different motor neuron diseases. Neurobiology of Aging 2014 May; 35(5): 1214.e1-6

Rosenbohm A, Kassubek J, Weydt P, **Marroquin N**, Volk AE, Kubisch C, Huppertz HJ, Weber M, Andersen PM, Weishaupt JH, Ludolph AC (2014): The ALS Schwaben Register Group. Can lesions to the motor cortex induce amyotrophic lateral sclerosis? Journal of Neurology 2014 Feb; 261(2): 283-90

Nagel SA1, Keuper A1, **Zagotta I**, **Enlunda E**, Rupereza AI, Debatin KM, Wabitscha M, Fischer-Posovszky P (2014): Up-regulation of Bcl-2 during adipogenesis mediates apoptosis resistance in human adipocytes. Molecular and Cellular Endocrinology, Volume 382, Issue 1, 25 January 2014, Pages 368–376

Palesch D, Khalid M, Stürzel CM, Münch J (2014): How can Xenotropic murine leukemia virus-related virus (XMRV) contamination be prevented? Susceptibility of XMRV to alcohol-based disinfectants and its environmental stability. Appl Environ Microbiol. 2014 Apr;80(8):2617-22. doi: 10.1128/AEM.04064-13.

Baecker T1, Mangus K, **Pfaender S**, **Chhabra R**, Boeckers TM, **Grabrucker AM** (2014): Loss of COMMD1 and copper overload disrupt Zn2+ homeostasis and influence an autismassociated pathway at glutamatergic synapses. Biometals 2014; 27(4):715-30.

Dragicevic E, **Poetschke C***, **Duda J***, Schlaudraff F, Lammel S, Schiemann J, Fauler M, Hetzel A, Watanabe M, Lujan R, Malenka R C, Striessnig J, Liss B (2014): Cav1.3 channels control D2-autoreceptor responses via NCS-1 in substantia nigra dopamine neurons. Brain: 137(Pt 8):2287-302. doi: 10.1093/brain/awu131.

Prill JM, Subr V, **Pasquarelli N**, Engler T, Hoffmeister A, Kochanek S, Ulbrich K and Kreppel, F (2014): Traceless Bioresponsive Shielding of Adenovirus Hexon with HPMA Copolymers Maintains Transduction Capacity In Vitro and In Vivo. PLoS One, 2014. 9(1):e82716.

Distler U, **Schmeisser MJ**, Pelosi A, **Reim D**, Kuharev J, Weiczner R, Baumgart J, Boeckers TM, Nitsch R, **Vogt J**, Tenzer S (2014): In-depth protein profiling of the postsynaptic density from mouse hippocampus using data-independent acquisition proteomics. Proteomics. 2014 Nov;14(21-22):2607-13. doi: 10.1002/pmic.201300520.

Richter J, **Bischof J**, Zaja M, Kohlhof H, Othersen O, Vitt D, Alscher V, Pospiech I, Garcia- Reyes B, Berg S, Leban J, Knippschild U (2014): Difluoro-dioxolo-benzoimidazol-benzamides as potent inhibitors of CK1delta and epsilon with nanomolar inhibitory activity on cancer cell proliferation. J Med Chem 2014, 57(19), 7933–7946.

Schneider V, Zhang L, Bullinger L, Rojewski M, Hofmann S, Wiesneth M, Schrezenmeier H, Götz M, Botzenhardt U, Barth TF, Döhner K, Döhner H, Greiner J (2014): Leukemic stem cells of acute myeloid leukemia patients carrying NPM1 mutation are candidates for targeted immunotherapy. Leukemia. 2014 Mar 28. doi: 10.1038/leu.2014.116.

Korbmacher JP, Michel C, Neubauer D, **Thompson K,** Mizaikoff B, Frick M, Dietl P, Wittekindt OH (2014): Amiloride sensitive fluid resorption in NCI-H441 lung epithelia depends on an apical Cl- conductance. Physiological Reports Vol.2:1. January 2014.

Vogel MJ, Xie L, Guan H, Tooze RM, Maier T, Kostezka U, Maier HJ, Holzmann K, Chan FC, Steidl C, Reichel JB, Weitzer CD, **Gehringer F**, Kick AB, Cesarman E, Roshal M, Gascoyne RD, Möller P, Wirth T, Ushmorov A (2014): FOXO1 repression contributes to block of plasma cell differentiation in classical Hodgkin lymphoma. Blood 124: 3118-3129.

Vogt J, Bengesser K, Claes KBM, Wimmer K, Mautner V-F, van Minkelen R, Legius E, Brems H, Upadhyaya M, Högel J, Lazaro C, Rosenbaum T, Messiaen L, Cooper DN, Kehrer-Sawatzki H (2014): SVA retrotransposon insertion-associated deletion represents a novel mutational mechanism underlying large genomic copy number changes with non-recurrent breakpoints. Genome Biol. 2014 Jun 2;15(6):R80. doi: 10.1186/gb-2014-15-6-r80.

Wehrle E, Fischer L, Bindl R, Heilmann A, Wehner T, Jakob F, Amling M & Ignatius A (2014): Ganzkoerpervibration fuehrt zur Beeintraechtigung der Frakturheilung in alten Maeusen, aber verbessert die Frakturheilung in alten, ovarektomierten Maeusen. Osteologie 2014.

Wehrle E, Wehner T, Heilmann A, Bindl R, Claes L, Jakob F, Amling M & Ignatius A (2014): Distinct frequency dependent effects of whole-body vibration on non-fractured bone and fracture healing in mice. J Orthop Res, doi: 10.1002/jor.22629.

Wehrle E, Liedert A, Heilmann A, Wehner T, Bindl R, Fischer L, **Haffner-Luntzer M**, Jakob F, Schinke T, Amling M, Ignatius A (2014): The impact of low-magnitude high-frequency vibration on fracture healing is profoundly influenced by the oestrogen status in mice. Dis Model Mech. 2014 Nov 7. pii: dmm.018622.

Nagel SA, Keuper M, **Zagotta I**, **Enlund E**, Ruperez AI, Debatin KM, Wabitsch M, Fischer-Posovszky P (2014): Up-regulation of Bcl-2 during adipogenesis mediates apoptosis resistance in human adipocytes. Mol Cell Endocrinol. 2014 Jan 25;382(1):368-76.

Missios P, **Zhou Y**, Guachalla LM, von Figura G, Wegner A, Chakkarappan SR, Binz T, Gompf A, Hartleben G, Burkhalter MD, Wulff V, Günes C, Sattler RW, Song Z, Illig T, Klaus S, Böhm BO, Wenz T, Hiller K & Rudolph KL (2014): Glucose substitution prolongs maintenance of energy homeostasis and lifespan of telomere dysfunctional mice. Nature Communications 5.

Freischmidt A, Müller K, **Zondler L**, Weydt P, Volk AE, Božič AL, Walter M, Bonin M, Mayer B, von Arnim CA, Otto M, Dieterich C, Holzmann K, Andersen PM, Ludolph AC, **Danzer KM**, Weishaupt JH (2014): Serum microRNAs in patients with genetic amyotrophic lateral sclerosis and pre-manifest mutation carriers. Brain. 2014 Nov;137(Pt 11):2938-50. doi: 10.1093/brain/awu249.

Zondler L, Miller-Fleming L, Repici M, Gonçalves S, Tenreiro S, Rosado-Ramos R, Betzer C, Straatman KR, Jensen PH, Giorgini F, Outeiro TF (2014): DJ-1 interactions with α-synuclein attenuate aggregation and cellular toxicity in models of Parkinson's disease. Cell Death Dis. 2014 Jul 24;5:e1350.

2015

Anastasiadou S, Liebenehm S, Sinske D, **Meyer Zu Reckendorf C**, Moepps B, Nordheim A, Knöll B (2015): Neuronal expression of the transcription factor serum response factor modulates myelination in a mouse multiple sclerosis model. Glia. 2015 Jun;63(6):958-76. doi: 10.1002/glia.22794.

Bergareche A*, **Bednarz M***, Sánchez E, Krebs CE, Ruiz-Martinez J, De la Riva P, Makarov V, Gorostidi A, Jurkat-Rott K, Marti-Masso JF, Paisán-Ruiz, C (2015): SCN4A pore mutation pathogenetically contributes to autosomal dominant essential tremor and may increase susceptibility to epilepsy. Human Molecular Genetics, (October), ddv410. http://doi.org/10.1093/hmg/ddv410; (*equal contribution).

Molt S, **Bührdel JB**, Yakovlev S, Schein P, Orfanos Z, Kirfel G, Winter L, Wiche G, van der Ven PF, Rottbauer W, Just S, Belkin AM, Fürst DO. J (2015): Aciculin interacts with filamin C and Xin and is essential for myofibril assembly, remodeling and maintenance. Cell Sci. 2014 Aug 15;127(Pt 16):3578-92.

Bührdel JB1, **Hirth S1**, Kessler M1, Westphal S1, **Forster M1**, Manta L1, Wiche G2, Schoser B3, Schessl J3, Schröder R4, Clemen CS5, Eichinger L5, Fürst DO6, van der Ven PF6, Rottbauer W7, Just S8 (2015): In vivo characterization of human myofibrillar myopathy genes in zebrafish. Biochem Biophys Res Commun. 2015 May 29;461(2):217-23.

Cappadona I1, Villinger C2, Schutzius G1, Mertens T1, von Einem J3 (2015): The human cytomegalovirus pUL47 modulates tegumentation and capsid accumulation at the viral assembly complex. J Virol. 2015 Jul;89(14):7314-28.

Chhabra R, Tosi G, **Grabrucker AM1** (2015): Emerging Use of Nanotechnology in the Treatment of Neurological Disorders. Curr Pharm Des. 2015;21(22):3111-30.

Chhabra R, Ruozi B, Vilella A, Belletti D, Mangus K, **Pfaender S**, Sarowar T, Boeckers TM, Zoli M, Forni F, Vandelli MA, Tosi G, **Grabrucker AM1** (2015): Application of Polymeric Nanoparticles for CNS Targeted Zinc Delivery In Vivo. CNS Neurol Disord Drug Targets. 2015;14(8):1041-53.

Ozfiliz P1, Kizilboga T1, **Demir S1**, Alkurt G1, Palavan-Unsal N2, Arisan ED2, Dinler-Doganay G1 (2015): Bag-1 promotes cell survival through c-Myc-mediated ODC upregulation that is not preferred under apoptotic stimuli in MCF-7 cells. Cell Biochem Funct. 2015 Jul;33(5):293-307.

Duda J, Fauler M, Gruendemann J and Liss B (2015): Cell-specific gene expression analysis in Parkinson's disease: tailored protocols for quantification of mRNA and miRNA levels in dopamine neurons from post mortem human midbrains by combining UV-laser microdissection and RT-qPCR techniques. Methods in Molecular Biology, in press.

Krabbe S, **Duda J,** Schiemann J, **Poetschke C**, Schneider G, Kandel E.R, Liss B, Roeper J, Simpson E.H (2015): Increased dopamine D2 receptor activity in the striatum alters the firing pattern of dopamine neurons in the ventral tegmental area. PNAS; published ahead of print February 9.

Miklavc P, **Ehinger K**, Sultan A, Felder T, Paul P, Gottschalk KE and Frick M (2015): Actin depolymerisation and crosslinking join forces with myosin II to contract actin coats on fused secretory vesicles. J. Cell Sci. 128:1193–203.

Feiler MS, Strobel B, Freischmidt A, **Helferich AM**, Kappel J, Brewer BM, Deyu L, Thal DR, Walther P, Ludolph AC, **Danzer KM**, Weishaupt JH (2015): TDP-43 is intercellularly transmitted across axon terminals. J Cell Biol. 2015 Nov 23;211(4):897-911.

Freischmidt A, Schöpflin M, **Feiler MS**, Fleck A, Ludolph AC, Weishaupt JH (2015): Profilin 1 with the amyotrophic lateral sclerosis associated mutation T109M displays unaltered actin binding and does not affect the actin cytoskeleton. BMC Neurosci. 2015 Nov 16;16(1):77.

Kunadt M, Eckermann K, Stuendl A, Gong J, Russo B, Strauss K, Rai S, Kügler S, Falomir Lockhart L, Schwalbe M, Krumova P, Oliveira LM, Bähr M, Möbius W, Levin J, Giese A, Kruse N, Mollenhauer B, Geiss-Friedlander R, Ludolph AC, Freischmidt A, **Feiler MS**, **Danzer KM**, Zweckstetter M, Jovin TM, Simons M, Weishaupt JH, Schneider A (2015): Extracellular vesicle sorting of α-Synuclein is regulated by sumoylation. Acta Neuropathol. 2015 May;129(5):695-713

Fischer S1,2, Paul AJ3, Wagner A3,4, Mathias S3,4, Geiss M3,4, Schandock F3,4, Domnowski M3,4, Zimmermann J3,4, Handrick R3, Hesse F3, Otte K3 (2015): miR-2861 as novel HDAC5 inhibitor in CHO cells enhances productivity while maintaining product quality. Biotechnol Bioeng. 2015 Oct;112(10):2142-53.

Fischer S, Handrick R, Aschrafi A, Otte K (2015): Unveiling the principle of microRNA-mediated redundancy in cellular pathway regulation. RNA Biol. 2015;12(3):238-47.

Barth H, **Fischer S**, Möglich A and Förtsch C (2015): Clostridial C3 toxins target monocytes/macrophages and modulate their functions. Front. Immunol. 6:339.

Wang T, Zabarska N, Wu Y, Lamla M, **Fischer S**, Monczak K, Ng DYW, Rau S and Weil T (2015): Receptor selective ruthenium-somatostatin photosensitizer for cancer targeted photodynamic applications. Chem. Commun. 51:12552-12555.

Halbedl S, Schoen M, **Feiler MS**, Boeckers TM, **Schmeisser MJ**. Shank3 is localized in axons and presynaptic specializations of developing hippocampal neurons and involved in the modulation of NMDA receptor levels at axon terminals. J Neurochem. 2016 Jan 4.

Halbgebauer S, Haussmann U, Klafki H, Tumani H, Wiltfang J and Otto M (2015): Capillary isoelectric focusing immunoassay as a new nanoscale approach for the detection of oligoclonal bands. Electrophoresis. 2015; 36:355-62.

Helferich AM, Ruf WP, **Grozdanov V**, Freischmidt A, **Feiler MS**, **Zondler L**, Ludolph AC, Weishaupt JH, McLean PJ, **Danzer KM** (2015): α-synuclein interacts with SOD1 and promotes its oligomerization. Mol Neurodegener. 2015 Dec 8;10:66.

Hempel A, and **Kühl SJ** (2015): Comparative expression analysis of cysteine-rich intestinal protein family members crip 1, 2 and 3 during Xenopus laevis embryogenesis. Int J Dev Biol. 2014;58(10-12):841-9.

Hering T, Birth N, Taanman JW, Orth M (2015): Selective striatal mtDNA depletion in end-stage Huntington's disease R6/2 mice. Experimental neurology 266C:22-29 (2015).

Zebrowski DC, Vergarajauregui S, Wu CC, Piatkowski T, Becker R, Leone M, **Hirth S**, Ricciardi F, Falk N, Giessl A, Just S, Braun T, Weidinger G, Engel FB (2015): Developmental alterations in centrosome integrity contribute to the post-mitotic state of mammalian cardiomyocytes. Elife. 2015 Aug 6;4

Walker MP, Stopford CM, Cederlund M, Fang F, **Jahn C**, Rabinowitz AD, Goldfarb D, Graham DM, Yan F, Deal AM, et al. (2015): FOXP1 potentiates Wnt/beta-catenin signaling in diffuse large B cell lymphoma. Science signaling 8, ra12.

Wehner D*, **Jahn C***, and Weidinger G (2015): Use of the TetON System to Study Molecular Mechanisms of Zebrafish Regeneration. Journal of visualized experiments : JoVE, e52756.

Kallert S, Zenk SF2, Walther P3, Grieshober M4, Weil T5, Stenger S6 (2015): Liposomal delivery of lipoarabinomannan triggers Mycobacterium tuberculosis specific T-cells. Tuberculosis (Edinb). 2015 Jul;95(4):452-62.

Dolnik A, **Kanwal N**, Mackert S2, **Halbedl S**, Proepper C, Bockmann J, Schoen M, Boeckers TM, **Kühl SJ**, **Schmeisser MJ** (2015): Sipa1l3/SPAR3 is targeted to postsynaptic specializations and interacts with the Fezzin ProSAPiP1/Lzts3. Journal of Neurochemistry 2015 Sep 14.

Kemmler J, Bindl R, McCook O, Wagner F, Gröger M, Wagner K, Scheuerle A, Radermacher P, Ignatius A (2015): Notification of Formal Acceptance for PONE-D-15-11658R2 : *Exposure to 100% oxygen abolishes the impairment of fracture healing after thoracic trauma. PLoS One. 2015 Jul 6;10(7):e0131194.

Lump E, Castellano LM, Meier C, Seeliger J, Erwin N, Sperlich B, Stürzel CM, Usmani S, Hammond RM, von Einem J, Gerold G, Kreppel F, Bravo-Rodriguez K, Pietschmann T, Holmes VM, Palesch D, Zirafi O, Weissman D, Sowislok A, Wettig B, Heid C, Kirchhoff F, Weil T, Klärner FG, Schrader T, Bitan G, Sanchez-Garcia E, Winter R, Shorter J, Münch J (2015): A molecular tweezer antagonizes seminal amyloids and HIV infection. eLife. doi: 10.7554/eLife.05397.

Groß A, Rödel K, Kneidl B, Donhauser N, Mössl M, **Lump E**, Münch J, Schmidt B, Eichler J (2015): Enhancement and Induction of HIV-1 Infection through an Assembled Peptide Derived from the CD4 Binding Site of gp120. ChemBioChem.16(3):446-54.

McLaren PJ, Gawanbacht A, Pyndiah N, Krapp C, **Hotter D**, Kluge SF, Götz N, Heilmann J, **Mack K**, Sauter D, Thompson D, Perreaud J, Rausell A, Munoz M, Ciuffi A, Kirchhoff F, Telenti A (2015): Identification of potential HIV restriction factors by combining evolutionary genomic signatures with functional analyses. Retrovirology. 2015 May 16;12:41.

Kluge SF1, **Mack K1,** Iyer SS2, Pujol FM3, Heigele A1, Learn GH2, Usmani SM1, Sauter D1, **Joas S1**, **Hotter D1**, Bibollet-Ruche F2, Plenderleith LJ4, Peeters M5, Geyer M6, Sharp PM4, Fackler OT3, Hahn BH7, Kirchhoff F8 (2015): Nef proteins of epidemic HIV-1 group O strains antagonize human tetherin. Cell Host Microbe. 2014 Nov 12;16(5):639-50.

Hübers A, Just W, Rosenbohm A, Müller K, **Marroquin N**, Goebel I, Högel J, Thiele H, Altmüller J, Nürnberg P, Weishaupt JH, Kubisch C, Ludolph AC, Volk AE (2015): De novo FUS mutations are the most frequent genetic cause in early onset German ALS patients. Neurobiol Aging. 2015 Nov;36(11):3117.e1-6.

Freischmidt A*, Wieland T*, Richter B*, Ruf W*, Schaeffer V, Müller K, **Marroquin N**, Nordin F, Hübers A, Weydt P, Pinto S, Press R, Millecamps S, Molko N, Bernard E, Desnuelle C, Soriani MH, Dorst D, Graf E, Nordström U, **Feiler MS**, Putz S, Boeckers TM, Meyer T, Winkler AS, Winkelman J, de Carvalho M, Thal DR, Otto M, Brännström T, Volk AE, Kursula P, **Danzer KM**, Lichtner P, Dikic I, Meitinger T, Ludolph AC, Strom TM**, Andersen PM**, Weishaupt JH** (2015): Haploinsufficiency of TBK1 causes familial amyotrophic lateral sclerosis and frontotemporal dementia. Nat Neurosci. 2015 May;18(5):631-6.

Marroquin N*, Stranz S*, Müller K, Wieland T, Ruf WP, **Brockmann SJ**, **Danzer KM**, Hübers A, Weydt P, Meitinger T, Strom TM, Rosenbohm A, Ludolph AC, Weishaupt JH. Screening for CHCHD10 mutations in a large cohort of sporadic ALS patients: No evidence for pathogenicity of the p.P34S variant. Brain 2015 Sep 11. pii: awv218

Lucas A, Lucas M, Strhyn A, Keane NM, McKinnon E, Pavlos R, Moran EM, **Meyer-Pannwitt V**, Gaudieri S, D'Orsogna L, Kalams S, Ostrov DA, Buus S, Peters B, Mallal S, Phillips E (2015): Abacavir-reactive memory T cells are present in drug naïve individuals. (2015) PLoS One. 10,e0117160.

Mohr KB, Zirafi O, Hennies M, Wiese S, Kirchhoff F, Münch J (2015): Sandwich enzyme-linked immunosorbent assay for the quantification of human serum albumin fragment 408-423 in bodily fluids. Anal Biochem 476: 29-35 (2015).

Zirafi O, Kim KA, Ständker L, **Mohr KB**, Sauter D, Heigele A, Kluge SF, Wiercinska E, Chudziak D, Richter R, Moepps B, Gierschik P, Vas V, Geiger H, Lamla M, Weil T, Burster T, Zgraja A, Daubeuf F, Frossard N, Hachet-Haas M, Heunisch F, Reichetzeder C, Galzi JL, Pérez-Castells J, Canales-Mayordomo A, Jiménez-Barbero J, Giménez-Gallego G, Schneider M, Shorter J, Telenti A, Hocher B, Forssmann WG, Bönig H, Kirchhoff F, Münch J (2015): Discovery and characterization of an endogenous CXCR4 antagonist. Cell Reports 11: 1–11 (2015).

Osswald A, Westermann C, Sun Z, Riedel CU (2015): A Phytase-Based Reporter System for Identification of Functional Secretion Signals in Bifidobacteria PLoS One. 2015 Jun 18;10(6):e0128802.

Pasquarelli N, Porazik C, Hanselmann J, Weydt P, Ferger B and Witting A (2015): Comparative biochemical characterization of the monoacylglycerol lipase inhibitor KML29 in brain, spinal cord, liver, spleen, fat and muscle tissue. Neuropharmacology, 2015. 91:148-156.

Qin R, Schmid H, Muenzberg C, Maass U, Krndija D, Adler G, Seufferlein T, Liedert A, Ignatius A, Oswald F, Eiseler T and von Wichert G (2015): Phosphorylation and Turnover of Paxillin in Focal Contacts is Controlled by Force and Defines the Dynamic State of the Adhesion Site, Cytoskeleton, February 2015 72:101-112.

Richter J, Ullah K, Xu P, Alscher V, Blatz A, Peifer C, Halekotte J, Leban J, Vitt D, Holzmann K, Bakulev V, Pinna L, Henne-Bruns D, Hillenbrand A, Kornmann M, Leithäuser F, Bischof J, Knippschild U (2015): Effects of altered expression and activity levels of CK1δ and ε on tumor growth and survival of colorectal cancer patients. Int J Cancer 2015, 136(12), 2799–2810.

Winkler BS, Oltmer F, **Richter J**, et al (2015): CK1δ in lymphoma: gene expression and mutation analyses and validation of CK1δ kinase activity for therapeutic application. Front Cell Dev Biol 3:9.

Winkler BS, Oltmer F, **Richter J, Bischof J**, Xu P, Burster T, Leithäuser F and Knippschild U (2015): CK1δ in lymphoma: gene expression and mutation analyses and validation of CK1δ kinase activity for therapeutic application. Front Cell Dev Biol 2015; 3(9).

Abderrazak A, Couchie D, Mahmood DFD, Elhage R, Vindis C, Laffargue M, Matéo V, Büchele B, **Ayala MR,** El Gaafary M, Syrovets T, Mohamed-Nace P (2015): Anti-Inflammatory and Antiatherogenic Effects of the NLRP3 Inflammasome Inhibitor Arglabin in ApoE2 .Ki Mice Fed a High-Fat Diet. Circulation. 2015; 1061–1070.

Schnell L, **Dmochewitz-Kück L**, Feigl P, Montecucco C, Barth H (2015): Thioredoxin reductase inhibitor auranofin prevents membrane transport of diphtheria toxin into the cytosol and protects human cells from intoxication. Toxicon doi:10.1016/j.toxicon.2015.04.012.

Stiefel F1,2, Paul AJ1, Jacopo T3, Sgueglia A3, **Stützle M1**,2, Herold EM4, Hesse F1 (2015): The influence of bisphenol A on mammalian cell cultivation. Appl Microbiol Biotechnol. 2015 Sep 18.

Diendorfer AB, Hackl M, Klanert G, Jadhav V, Reithofer M, **Stiefel F**, Hesse F, Grillari J, Borth N (2015): Annotation of additional evolutionary conserved microRNA in CHO cells from updated genomic data. Biotechnol Bioeng. 2015 Feb 16.

Stiefel F, Fischer S et al. (2015): Non-coding RNAs, post-transcriptional RNA Operons and Chinese hamster ovary cells. Review. Pharmaceutical Bioprocessing 04/2015; 3(3):1-21.

Eschbach J, **von Einem B**, Müller K, **Bayer H**, **Scheffold A**, Morrison BE, Rudolph KL, Thal DR, Witting A, Weydt P, Otto M, Fauler M, Liss B, McLean PJ, Spada AR, Ludolph AC, Weishaupt JH, **Danzer KM** (2015): Mutual exacerbation of peroxisome proliferator-activated receptor γ coactivator 1α deregulation and α-synuclein oligomerization, Ann Neurol. 2015 Jan.

von Einem B, **Wahler A**, **Schips T**, Serrano-Pozo A, Proepper C, Boeckers TM, Rueck A, Wirth T, Hyman BT, **Danzer KM**, Thal DR, von Arnim CA (2015): 3 GGA proteins alter APP processing through interaction of their GAE-domain with BACE1., Neurobiol. Aging PLoS One. 2015 Jun 8;10(6):e0129047.

Freischmidt A, Müller K, **Zondler L**, Weydt P, Mayer B, von Arnim CA, Hübers A, Dorst J, Otto M, Holzmann K, Ludolph AC, **Danzer KM**, Weishaupt JH (2015): Serum microRNAs in sporadic amyotrophic lateral sclerosis. Neurobiol Aging. 2015 Sep;36(9):2660.e15-20.

2016

Bliederhaeuser C, **Grozdanov V**, **Speidel A**, **Zondler L**, Ruf WP, **Bayer H**, **Kiechle M**, **Feiler MS**, Freischmidt A, Brenner D, Witting A, Hengerer B, Fändrich M, Ludolph AC, Weishaupt JH, Gillardon F, **Danzer KM** (2016): Age-dependent defects of alpha-synuclein oligomer uptake in microglia and monocytes. Acta Neuropathol. 2016 Mar;131(3):379-91.

Stiefel F, Paul AJ, Jacopo T, Sgueglia A, **Stützle M**, Herold EM, et al. (2016): The influence of bisphenol A on mammalian cell cultivation. Appl. Microbiol. Biotechnol. 2016;100:113–24.

Nagler M[1], Palkowitsch L[2], Rading S[1], Moepps B[3], Karsak M[4] (2016): Cannabinoid receptor 2 expression modulates Gβ1γ2 protein interaction with the activator of G protein signalling 2/dynein light chain protein Tctex-1. Biochem Pharmacol. 2016 Jan 1;99:60-72.

Zondler L, Müller K, **Khalaji S, Bliederhäuser C**, Ruf WP, **Grozdanov V**, Thiemann M, Fundel-Clemes K, Freischmidt A, Holzmann K, Strobel B, Weydt P, Witting A, Thal DR, **Helferich AM**, Hengerer B, Gottschalk KE, Hill O, Kluge M, Ludolph AC, **Danzer KM**, Weishaupt JH (2016). Peripheral monocytes are functionally altered and invade the CNS in ALS patients. Acta Neuropathologica

Imprint

Publisher
International Graduate School
in Molecular Medicine Ulm
Ulm University
Albert Einstein Allee 11
O25/424-425
89081 Ulm · Germany
Tel. +49 (0)731-50-36290
Fax +49 (0)731-50-36292
igradu@uni-ulm.de
www.uni-ulm.de/mm

2016

Editors
PD Dr. Dieter Brockmann
Prof. Dr. Michael Kühl
Bettina Braun, Int. Dipl. Betriebswirtin

Design, organization
Gabriele Stautner, Artifox Communication Design Ulm
stautner@artifox.com, www.artifox.com

Proof reading
John McKeon, Artifox Communication Design Ulm

Photos (unless otherwise specified)
Artifox Communication Design Ulm
Medical Faculty of Ulm University
University Medical Center Ulm

We thank the people of the institutes and departments of Ulm University
and of the University Medical Center Ulm for their support.

IGradU

ulm university universität ulm

International Graduate School
in Molecular Medicine Ulm
IGradU
Ulm University
Albert Einstein Allee
89081 Ulm · Germany
Tel. +49 (0)731-50-36290
Fax +49 (0)731-50-36292
igradu@uni-ulm.de
www.uni-ulm.de/mm