

Dear CRC 1149 members,

The second funding period is only a few months old, and the CRC already has some highlights we would like to report. One is the Gender Equality Award by the University of Ulm the CRC obtained, and the reelection of our speaker Professor Florian Gebhard and representatives Professor Markus Huber-Lang and Professor Anita Ignatius. Furthermore, there are new Gender fundings.

I wish you all the best.

Miriam Kalbitz

New PIs in the second funding period of the CRC1149



Leda Dimou, Ph.D., is Professor for Molecular and Translational Neuroscience at the Department of Neurology of the Ulm University since November 2016. She studied Biology in the University of Heidelberg and performed her PhD in the lab of Klaus Nave in the same University and the Max-Planck-Institute for Experimental Medicine in Göttingen. After a postdoc in Martin Schwab's lab in Zurich working on spinal cord injury, she joined the lab of Magdalena Götz at the LMU (Munich), where she also became a group leader.

Leda Dimou is interested on oligodendrogenesis and specifically in the function and differentiation potential of oligodendrocyte progenitor cells (NG2-glia) in the adult brain as well as their interaction with other glial cells and especially microglia. She generated novel transgenic mice and could demonstrate that NG2-glia are very heterogeneous and they can differentiate into mature, myelinating oligodendrocytes in the intact adult cortex in a spatial matter. Using fate mapping, transplantation techniques, FACS, transcriptome analysis and *in vivo* 2-photon microscopy, she is studying the behavior and potential of NG2-glia in the intact brain, after injury and in neurodegenerative diseases. Leda Dimou is PI of the new project **A08-N** Role of NG2-glia in different injury paradigms.



Dr. Clair Hartmann has been a resident in the Department of Anesthesiology at the University Hospital Ulm since 2014. She studied medicine in Ulm from 2007-2014, completing her medical thesis, "Tbx3 Direct's Cell-Fate Decision towards Mesendoderm", with summa cum laude in the Laboratory of Prof. Dr. A. Kleger. From 2015-2018 she performed a Post Doc in the Institute for Anesthesiological Pathophysiology and Process Engineering at the University Hospital in Ulm (Prof. Dr. Dr. P. Radermacher). Her primary focus lies on the impact of hydrogen sulfide in critical illness but she is also doing research in the immunometabolism field. She is interested in characterizing how and to which extent the innate and adaptive immune system is

activated during the acute phase of a defined porcine acute subdural hematoma and subsequent hemorrhagic shock, followed by intensive care therapy for 50h with/without hyperoxia treatment during the first 12h. In the long-term she plans to study whether changes within the energy metabolism of circulating immune cells correlate with the severity of disease and thus could be used as a bioenergetic biomarker. She is therefore Co-PI of **B03**, together with Peter Radermacher.



Dr. Melanie Haffner-Luntzer is a Principal Investigator in the Institute of Orthopaedic Research and Biomechanics at the University of Ulm (head of institute: Prof. Anita Ignatius). She received her bachelor's and master's degree in the field of molecular medicine from the University of Ulm in 2009 and 2011. In March 2015, she finished her PhD thesis with the topic "The Role of Midkine During Fracture Healing" within the International Graduate School for Molecular Medicine. Dr. Haffner-Luntzer's research focuses on molecular mechanisms involved in fracture healing, bone homeostasis and osteoporosis. She is a member of the European Calcified Tissue Society, the Orthopaedic Research Society, the American Society for Bone and Mineral Research, the European Society for Biomechanics, the AOTrauma Foundation, the German Society for Trauma Surgery and the German Society for Biomechanics. In 2019, she was elected as a member-at-large of the ORS International Section for Fracture Repair. Besides several travel and poster awards, in 2014, she and her colleagues received the prestigious Wilhelm-Roux award from the German Society of Orthopaedics and Trauma Surgery for her work investigating the influence of Midkine-deficiency on fracture healing in mice. In 2016, she was awarded with the "best basic research paper award" from the German Society of Orthopaedics and Trauma Surgery, the price carries a value of 20,000 Euro. In 2018, she received the New Investigators Recognition Award from the ORS for her work investigating the influence of epigenetic regulators on bone homeostasis. In 2019, she received the ORS ISFR award for the best podium presentation. Dr. Melanie Haffner-Luntzer received funding from the German Research Foundation, the AOTrauma Germany Foundation and the Elsbeth-Bonhoff-Foundation for Osteoporosis Research. Together with Prof. Reber Dr. Melanie Haffner-Luntzer is PI of the new project **B06-N**: Effects of psychosocial trauma on bone homeostasis and fracture healing.



Stefan Reber, Ph.D., is Professor for Molecular Psychosomatics at the Department of Psychosomatic Medicine and Psychotherapy at Ulm University Medical Centre since 2013. He studied Biology and Chemistry at the University of Bayreuth (Germany) and received his PhD at the University of Regensburg (Germany) for his work on the Psychoneuroimmunology of chronic psychosocial stress in 2007. Prof. Reber's current research is focused on extending the present knowledge on the mechanisms underlying stress-induced somatic and mental pathologies as well as individual differences in stress resilience, and to use this mechanistic knowledge for the development of novel strategies in terms of stress protection. Prof. Reber has an H-index of 25 (Google Scholar), has published over 50 peer-reviewed articles and book

chapters and received, amongst others, the Ernst and Berta Scharrer Award of the German Endocrine Society (2010) and the Curt P. Richter Award of the International Society for Psychoneuroendocrinology (2016).

Together with Dr. Haffner-Luntzer Prof. Reber is PI of the new project **B06-N**: Effects of psychosocial trauma on bone homeostasis and fracture healing.



Dr. Sabine Vettorazzi is deputy group leader in the Institute of Comparative Molecular Endocrinology at Ulm University since 2016. She studied Biology at the Friedrich Schiller University in Jena (Germany) from 2003-2008. She did her PhD at the Leibniz Institute on Aging in Jena (Germany) about the regulation of inflammatory mechanism by the glucocorticoid receptor from 2009 – 2013. As a Postdoc she started in Ulm at the Institute of Comparative Molecular Endocrinology. Her research is focused on the control of inflammatory diseases (lung and systemic) by the glucocorticoid receptor that mediates anti-inflammatory actions.

This receptor is activated by glucocorticoids which are in use to treat acute and chronic inflammatory diseases in patients. Investigating the underlying mechanisms of the synergism from pro- and anti-inflammatory mediators that are both activated simultaneously during inflammation she aims at the identification of new therapeutic targets to regulate inflammation. She published over 20 peer-reviewed articles and reviews in high impact journals like nature communications. Dr. Sabine Vettorazzi received the Hugo Schottmüller award from the German Sepsis Society for outstanding publication in basic science research of sepsis for young scientists (2016) and was nominated for the Academics Young Scientist Award (newspaper “Die Zeit” 2016). In 2017 she was a finalist of the New Investigator Award Competition at the Congress of the European Shock Society. She received various third party funds and travel support as well as technical assistance support during pregnancy from the SFB 1149 (2017). Together with Dr. Martin Wepler Dr. Sabine Vettorazzi is PI of the new project **B07-N**: Effects of impaired glucocorticoid receptor function in hemorrhagic shock-induced lung injury with pre-existing cigarette smoke-induced chronic obstructive pulmonary disease.



Dr. Martin Wepler is an Anesthesiologist at the Department of Anesthesiology at the University Hospital Ulm. He studied medicine in Rostock and Ulm (Germany) from 2001-2007. From 2005-2006 he did his doctoral thesis about the “Injection of insulin and pain sensation in children with diabetes – a prospective, controlled, non-interventional, and observational study” at the University of Ulm (Prof. Beate Karges). While he was working as an Anesthesiologist at the University Hospital in Ulm since 2008, he got a research fellowship at the Institute for Anesthesiological Pathophysiology and Process Engineering at the University Hospital in Ulm,

Germany, led by Prof. Dr. Dr. Peter Radermacher in 2012. From September 2013 to September 2016 he worked as a research fellow at the Anesthesia Center for Critical Care Research at the Department of Anesthesia and Critical Care, Massachusetts General Hospital and Harvard Medical School, Boston, MA, led by Prof. Dr. Warren M. Zapol. His research focused on the „Effects of combining selective PDE9 inhibition with

inhaled nitric oxide on pulmonary gas exchange, mechanics, inflammation and lung injury in a murine model of ventilator induced lung injury“ an was supported by a research fellowship from the German Research Foundation (DFG). Since October 2016 he is working as research fellow at the Institute of Anesthesiological Pathophysiology and Process Engineering at the University Hospital in Ulm, Germany, (GEROK Position within the CRC1149 funded by the DFG) and as an Anesthesiologist at the University Hospital Ulm. He was the winner of the Poster Award Competition at the XVIth I Congress of the European Shock Society, September 13-15 2017, Paris, France and as a last author at the 39th International Symposium on Intensive Care and Emergency Medicine, March 19-22, 2019 in Brussels, Belgium. Together with Dr. Sabine Vettorazzi, Dr. Martin Wepler is the PI of the new project **B07-N**: Effects of impaired glucocorticoid receptor function in hemorrhagic shock-induced lung injury with pre-existing cigarette smoke-induced chronic obstructive pulmonary disease.



Hubert Schrezenmeier, M.D., is Professor of Transfusion Medicine at the Institute of Transfusion Medicine, Ulm University Medical Center and Medical Director of the Institute of Clinical Transfusion Medicine and Immunogenetics, a joint entity of University Hospital Ulm and the German Red Cross Blood Transfusion Service Baden-Württemberg-Hessen. He is board certified in Tansfusion Medicine and Internal Medicine, Hematology and Medical Oncology. His main topics of research are cellular therapy, stem cell transplantation and molecular diagnostics.

Hubert Schrezenmeier has long-standing experience in development and characterization of cellular therapy products. He has been work package leader in two European consortia on MSC (CASCADE: Cultivated Adult Stem Cells as Alternative for Damaged Tissue, REBORNE: Regenerating Bone Defects Using New Biomedical Engineering Approaches) and is Work Package leader in the ongoing HORIZON2020 projects ORTHOUNION (Orthopedic randomized clinical trials with expanded bone marrow MSC and bioceramics versus autograft in long bone nonunions), ADIPOA2 (Autologous ASC in the treatment of mild to moderate osteoarthritis) and MAXIBONE (Personalised maxillofacial bone regeneration). With his team and the partners in cooperative projects he developed efficient ex vivo expansion methods for MSC and ASC. Expanded cells have been characterized for safety and proficiency and finally manufacturing license and regulatory approval for clinical trials of MSC have been obtained. He authored or co-authored more than 240 peer-reviewed publications on MSC, mechanisms and treatment of bone marrow failure syndromes, immunomodulation, and hematopoietic stem cell transplantation (H-index 69; Google Scholar). Currently he is a Board Member of the German Society of Transfusion Medicine and Immunohematology and Member of the Editorial Board of Annals of Hematology, Transfusionsmedizin and Haemotherapie. He serves as member of the Ethical Committee of the University of Ulm. Together with Miriam Kalbitz he is Co-PI of the new project **C07-N**.



PD Dr. Miriam Kalbitz, MD, Functioning Senior Physician, head of trauma research laboratory at the Department of Trauma, Hand, Plastic and Reconstructive Surgery at Ulm University Medical Centre since 2006. She studied Medicine at the University of Ulm. In 2012 Dr. Kalbitz received board certification in Orthopedic and Trauma Surgery. 2012-2013 she investigated the role of the complement system in cardiac dysfunction during sepsis in the context of a research fellowship at the University of Michigan, Department of Pathology, in Prof. Dr. Peter Wards lab which was funded by the German Research Foundation (DFG). In October 2013 Dr. Kalbitz returned to the Department of Trauma, Hand, Plastic and Reconstructive Surgery at Ulm University and participated in the Bausteinprogramm, Else Kröner-Forschungskolleg and the Clinician Scientist Program of the Medical Faculty of the University of Ulm. In 2017 Dr. Kalbitz received post-doctoral lecture qualification and university teaching in Orthopedic Trauma Surgery at the University of Ulm for her work on the role of the complement system on cardiac dysfunction during sepsis. In 2015 Dr. Kalbitz received the Hugo-Schottmüller Award of the German Sepsis Society and the Günther Schlag Memorial Award of the Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, Vienna for her research in septic cardiomyopathy. Dr. Kalbitz's current research focus is the mechanisms underlying posttraumatic cardiac dysfunction. Together with Prof. Schrezenmeier Dr. Kalbitz is PI of the new project **C07-N: Cardiac function after trauma and MSC-based regenerative strategies**. Kalbitz/ Schrezenmeier.

Fall workshop Neu-Ulm

The annual fall workshop and CRC annual meeting was held in the Gasthof Hirsch in Neu-Ulm on Monday 10th of December 2018. One item of the agenda was to celebrate the granting of the second funding period of the CRC 1149. In a cosy atmosphere, selected old and new projects as well as the Z-projects were presented.

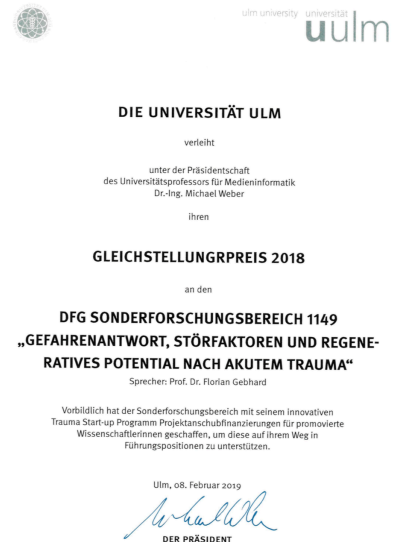
The researchers were highly motivated to start in the next funding period.



Gender Equality Award for the CRC

The CRC1149 obtained the Gender Equality Award of the University of Ulm due to the exemplarily innovative trauma start-up program for funding of graduated female researchers on their career path to leadership positions. The prize comprised an award sum of 2,500 Euros.

Since 2015 seven female researchers were funded by the start-up program of the CRC1149 with 10,000 Euro resulting in four projects included in the second funding period. The new projects were examined in the appraisal for the second funding period from excellent to outstanding. Furthermore the CRC supported female researchers during pregnancy and parental leave by the Pregnancy in Trauma Research (PRT) program. The proportion of women rose in the second funding period of the CRC from 18 to 32 percent.



Reelection of Professor Florian Gebhard as Speaker of the CRC1149

The count of votes in the election of the speaker, deputy speakers and steering committee of the CRC1149 resulted in the reelection of Professor Florian Gebhard as speaker, Professor Markus Huber-Lang and Professor Anita Ignatius as deputy speakers. For the new steering committee Professor Karin Scharffetter-Kochanek, Professor Stefan Reber, Professor Jan Tuckermann, Professor Thomas Wirth and Professor Leda Dimou-Rörentrop obtained the largest number of votes. 39 of the 55 members of the CRC voted, resulting a voter turnout of 70%.

Successful Orthopedic Research Society Annual Meeting in Austin, Texas



6 out of 10 contributions of the Institute of Orthopaedic Research and Biomechanics received scientific awards on the annual meeting of the American Orthopaedic Research Society (ORS) 2019. Four of those awards were granted to members of the CRC 1149:

Prof. Lutz Dürselen received the **Best Podium Award of the ORS Meniscus Section**, Dr. Verena Fischer was awarded with the **ORS/ON Foundation Education Grant** and the **Best Podium Award of the ORS International Section of Fracture Repair** was received for

the contribution “Chronic Psychosocial Stress Disturbs the Inflammatory Response and Enchondral Ossification after Bone Fracture via β -adrenoceptor Signaling”. Authors: **Melanie Haffner-Luntzer**, Sandra Foertsch, **Verena Fischer**, Katja Prystaz, Miriam Tschaffon, Yvonne Moedinger, **Anita Ignatius**, **Stefan O. Reber**. Furthermore, one poster from a cooperation project of Dr. Melanie Haffner-Luntzer and PD Dr. Miriam Kalbitz was presented.

Gender Equality Funding/ Start-up Funding

Dr. Melanie Haffner-Luntzer is supported by the Pregnancy in Trauma Research program to receive technical assistance for lab work during her pregnancy and parental leave.



Dr. Verena Fischer is supported by Startup Funding (10,000 Euro) of the CRC1149 in the lab of Prof. Anita Ignatius, Institute of Orthopaedic Research and Biomechanics. Her project entitled “Influence of S100A8/A9 primed MSCs on bone fracture healing” aims to investigate whether MSC priming with the DAMP molecule S100A8/A9 enhances critical size bone defect healing. The project will be conducted in cooperation with the group of Prof. Karin Scharffetter-Kochanek, Department of Dermatology and Allergology. Mice will receive a femoral critical size defect stabilized by an external fixator and primed and non-primed MSCs seeded in collagen gels will be applied at the fracture site. The success of bone formation will be evaluated by biomechanical, μ CT, histomorphometric and immunohistochemical analyses.



Tamara Merz (left), Institute for Pathophysiological Anesthesiology and Process Engineering received start-up funding (11,000 Euro) for the project “The role of hydrogen sulfide in circulatory shock-induced barrier dysfunction”.

Dr. Rebecca Halbgebaur (right), Institute of Clinical and Experimental Trauma Immunology received GENDER funding (14,400 Euro) for the project “Establishing and characterization of a murine model of blunt abdominal trauma”.



Research visit at the Orthopaedic Trauma Institute in San Francisco

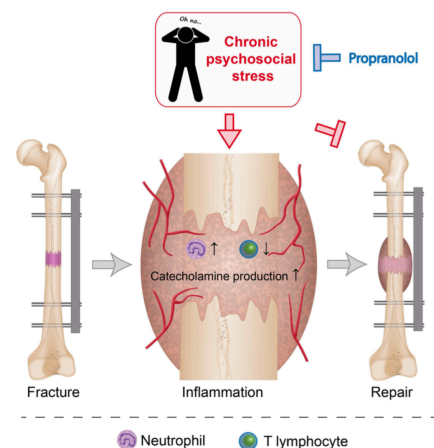


Supported by the Hertha-Nathorff-program of Ulm University, the two CRC1149 PIs PD Dr. Miriam Kalbitz and Dr. Melanie Haffner-Luntzer conducted a research visit at the Orthopaedic Trauma Institute (OTI), University of California San Francisco (UCSF) in January 2019. The aim of the visit was to establish a new clinically relevant osteoporotic hip fracture model in mice to investigate differences in fracture healing between young and aged mice. Furthermore, cardiac damage after fracture in young and aged mice and after combination of fracture and traumatic brain injury were the research focus. The OTI is home to the largest number of trauma fellowship trained surgeons in the US and has various research programs that include biomechanics, molecular biology of fracture healing and limb regeneration, and clinical research. The collaboration between the OTI, the Institute of Orthopaedic Research and Biomechanics and the Clinics for Trauma Surgery will help to answer important research questions in the context of the CRC1149.

Further Awards

Ms. Miriam Tschaffon received the **Best Graphical Abstract Award from the MuSkITYRs** (MuskuloSkeletal Interdisciplinary Translational Young Researchers) at the Osteologie conference 2019 for her work in the CRC1149 cooperation project together with the group of Prof. Stefan Reber.

Mr. Julius Mühleisen from the Institute of Comparative Molecular Endocrinology (Jan Tuckermann) was honored with an **Aegean Conference Travel Award** in recognition of an excellent research contribution. The award ceremony took place in the frame of the 7th International Conference of Osteoimmunology: Interactions of the Immune and Skeletal Systems (June 3-8, 2018 in Crete, Greece).
The CRC congratulates the winners most warmly for their excellent work!



Prof. Holger Barth from the Institute of Pharmacology and Toxicology have been re-elected as President of the German Society of Toxicology. The presidents new tenure will start in January 2020 and will last for 3 years.



Professor Dr. Holger Barth from the Institute for Pharmacology and Toxicology has been appointed to the scientific advisory panel of the research institutes for NBC-protection of the medical academy of the German Armed Forces. Congratulations!

Preisverleihung

Hugo-Schottmüller-Preis 2018



>> Gestiftet von der DSG

>> Verliehen an

Dr. biol. hum. Stefanie Denk

Institut für Klinische und Experimentelle Trauma-Immunologie, Universitätsklinikum Ulm

für ihre Arbeit

Complement C5a Functions as a Master Switch for the pH Balance in Neutrophils Exerting Fundamental Immunometabolic Effects.

J Immunol. 2017 Jun 15;198(12)



The German Sepsis Society awarded **Dr. Stefanie Denk** with the Hugo-Schottmüller Preis 2018 for her excellent Publication “Complement C5a Functions as a Master Switch for the pH Balance in Neutrophils Exerting Fundamental Immunometabolic Effects” published in the Journal of Immunology 2017. Congratulations!

Announcements

The **next CRC Retreat** will take place on May 20th- 21st 2019.



Location: Explorer Hotel Ötztal (www.explorer-hotels.com/oetztal)

We are happy to see you all there and discuss with you the recent achievements and outlook of the projects. Furthermore, the general meeting will be held in the context of the workshop.

Next seminar series 2019

39. SFB seminar

May 16th 2019

4 pm: "Asphyxia and hemorrhagic shock in a neonatal model"

PD Dr. Miriam Kalbitz

N27 Multimedia

40. SFB seminar

June 27th 2019

4 pm "New therapeutic targets in the early phase of TBI"

Dr. Dr. Francesco Roselli

N27 Multimedia

41. SFB seminar

July 18th 2019

4 pm "Bacterial toxins in pharmacology"

Prof. Dr. Holger Barth

N27 Multimedia

GEROK funding

Applications for GEROK funding are appreciated!

Selected New Publications

1. Biglarnia AR, **Huber-Lang M**, Mohlin C, Ekdahl KN, Nilsson B. The multifaceted role of complement in kidney transplantation. *Nat Rev Nephrol*. 2018 Dec;14(12):767-781.
2. Singh K, Camera E, Krug L, Basu A, Pandey RK, Munir S, Wlaschek M, Kochanek S, Schorpp-Kistner M, Picardo M, Angel P, Niemann C, Maity P, **Scharffetter-Kochanek K**. JunB defines functional and structural integrity of the epidermo-pilosebaceous unit in the skin. *Nat Commun*. 2018 Aug 24;9(1):3425.
3. Lee JW, Sicre de Fontbrune F, Wong Lee Lee L, Pessoa V, Gualandro S, Füreder W, Ptushkin V, Rottinghaus ST, Volles L, Shafner L, Aguzzi R, Pradhan R, **Schrezenmeier H**, Hill A. Ravulizumab (ALXN1210) vs eculizumab in adult patients with PNH naive to complement inhibitors: the 301 study. *Blood*. 2019 Feb 7;133(6):530-539.
4. Reisser M, Palmer A, Popp AP, Jahn C, **Weidinger G**, Gebhardt JCM. Single-molecule imaging correlates decreasing nuclear volume with increasing TF-chromatin associations during zebrafish development. *Nat Commun*. 2018 Dec 6;9(1):5218.
5. Owlarn S, Klenner F, Schmidt D, Rabert F, Tomasso A, Reuter H, Mulaw MA, Moritz S, Gentile L, **Weidinger G**, Bartscherer K. Generic wound signals initiate regeneration in missing-tissue contexts. *Nat Commun*. 2017 Dec 22;8(1):2282.
6. McNeer NA, Philip J, **Geiger H**, Ries RE, Lavallée VP, Walsh M, Shah M, Arora K, Emde AK, Robine N, Alonzo TA, Kolb EA, Gamis AS, Smith M, Gerhard DS, Guidry-Auvil J, Meshinchi S, Kentsis A. Genetic mechanisms of primary chemotherapy resistance in pediatric acute myeloid leukemia. *Leukemia*. 2019 Feb 13.
7. Ovadya Y, Landsberger T, Leins H, Vadai E, Gal H, Biran A, Yosef R, Sagiv A, Agrawal A, Shapira A, Windheim J, Tsoory M, Schirmbeck R, Amit I, **Geiger H**, Krizhanovsky V. Impaired immune surveillance accelerates accumulation of senescent cells and aging. *Nat Commun*. 2018 Dec 21;9(1):5435. doi: 10.1038/s41467-018-07825-3.
8. **Haffner-Luntzer M**, Foertsch S, Fischer V, Prystaz K, Tschaflon M, Mödinger Y, Bahney CS, Marcucio RS, Miclau T, **Ignatius A**, **Reber SO**. Chronic psychosocial stress compromises the immune response and endochondral ossification during bone fracture healing via β -AR signaling. *Proc Natl Acad Sci U S A*. 2019 Apr 4.