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Preface

University-based medicine provides optimal patient-care within the framework of state-of-the-art knowledge and aims at the same time to continuously develop this medical knowledge for its application in the future.

Innovation requires research and in particular the translation of scientific findings into clinical application as well as the analysis of clinical questions by employing methods and models of basic research.

Especially in Pediatric Oncology, the pioneer of interdiscliplinary and multimodal treatment of leukemias and tumors on the whole, further progress in the already relatively successful therapy of our patients is only possible through further research.

Also, the analysis and characterization of the fundamentals of rare diseases, the adaption of medical care to age-dependent factors like premature birth, and the prevention of metabolic and endocrinologic diseases require the combination of basic research, clinical research and innovative treatment strategies.

Research at our department is dedicated to these goals. With the establishment and successful conclusion of the DFG-funded clinical research unit “Regulation of Apoptosis and its Dysfunction in Human Diseases” our department has developed a profile in its field and within the Medical Faculty.

Currently, our department participates in two Collaborative Research Centers (SFB) of the German Research Foundation (DFG) at Ulm University, SFB 1074 “Experimental Models and Clinical Translation in Leukemia” (Prof. Debatin co-chair) and SFB 1149 “Danger Response, Disturbance Factors and Regenerative Potential after Acute Trauma”. Our department also participates in a research consortium funded by the state of Baden-Württemberg and Boehringer Ingelheim (BIU; coordinator Prof. Debatin).

With this report, we inform you about the focuses and developments during the last four years. Special thanks go to all employees that have contributed to this top-class research in a clinical setting.
Research Profile – Summary

Our research in Hematology and Oncology is dedicated to understanding the role of cell death (apoptosis) and cell death signaling in diseases, such as cancer, with the aim of developing new therapies from this knowledge. Our lab was involved in the early discovery of one of the key apoptosis signaling pathways (CD95/APO/Fas in 1989 and 1990), while identifying and initially describing its role in cancer therapy in 1996. A particular focus lies on strategies to overcome treatment resistance in leukemia, neuroblastoma and brain tumors. In doing so, we have addressed several issues dealing with apoptosis regulators and apoptosis signaling as prognostic factors and therapeutic targets, and have thereby contributed to the development of new drugs for cancer therapy. By using models of primary leukemias, we are in the process of analyzing aspects of leukemia stem cell function and apoptosis sensitivity of leukemia-initiating cells as well as parameters for treatment response and outcome in patients. The expertise of our work group has been introduced into the international study group (I-BMF) for the treatment of childhood leukemia. In the area of solid tumors, we investigate the molecular pathways which may provide novel therapeutic targets in glioblastoma by utilizing patient-derived tumor cells.

The Experimental Pediatric Oncology Section investigates the molecular pathogenesis and diagnosis of neuroblastoma and develops experimental therapy for neuroblastoma and acute lymphoblastic leukemia.

In the field of Non-malignant Hematological Diseases, we also investigate pathological processes and the underlying molecular alterations as a basis for the development of specific treatment strategies, especially in the area of congenital and acquired erythrocytoses/polycythemias, as well as rare metabolic defects associated with the disruption of hematopoiesis.

In the area of Stem cell transplantation and Immunology, our work groups have significantly contributed to the development of blood stem cell and bone marrow transplantations and have characterized the genetic origins of several forms of severe combined immune defects (SCID). In the early seventies one of the first ever bone marrow transplants
in children in Europe was performed at our hospital. Novel therapies, such as haploidentical stem cell transplantations, cell-based immunotherapies and, most recently, radioimmunotherapy-based conditioning for reduced toxicity during treatment of severe combined immune defects, congenital hematological disorders and leukemias, have since been developed. The work group at Ulm University is part of the federal network on primary immunodeficiencies.

The research areas of the Division of Pediatric Endocrinology include development and disturbances of the endocrine system, endocrine regulation of body weight and diabetes mellitus type 1 and type 2. The main focus of research projects lays in diseases going along with alterations in adipose tissue mass and function such as obesity and lipodystrophies and their comorbidities. On one hand the aim is to identify the underlying pathophysiology on the genetic, molecular, cellular, organ and systemic level. On the other hand, in clinical studies novel treatment options are evaluated.

The research of the Neonatology and Pediatric Intensive Care Section is dedicated to clinical studies related to primary care of neonates and preterm infants. Our center participates in a number of multicenter randomized trials, including the coordination of a European multicenter study on the use of inhalative NO treatment, and has initiated a study on permissive hypercapnia in very immature preterm infants.

In the Social Pediatrics and Child Neurology Section, we study the developmental prognosis of neonates after severe perinatal asphyxia and the long-term prognosis of premature babies of very low birth weight. We are assessing the influence of longchain polyunsaturated fatty acids on characteristics and cognition in attention-deficit/hyperactivity disorder (ADHD). Finally, we study the long term development and outpatient care of children with ADHD.
Research Groups

Glioblastoma Research

Heads: Prof. Klaus-Michael Debatin, Dr. Mike-Andrew Westhoff
Staff: Martina Maushart, Dr. Lisa Nonnenmacher, Christel Payer, Andrea Schuster

The main focus of our cancer therapy and apoptosis research lies with Glioblastoma which is among the most lethal tumours encountered in the clinic. It is the most frequent primary brain tumour in adults and is also not uncommon in children. Successful therapy, consisting of maximal safe surgical resection, radio- and chemotherapy, only extents life expectancy to 15 months.

Our research group focuses on three areas of interest:

■ The molecular features of Glioblastoma

Unusual for such an aggressive disease Glioblastoma has relatively few distinct mutations and other genetic alterations, presenting the researcher with few druggable targets. Among those is the PI3K signalling cascade that is activated in ~90% of all Glioblastoma. Understanding the role of this signalling network in different cell populations of the tumour and elucidating the therapeutic potential of pathway inhibition has led new therapeutic avenues implemented in our clinic. [1]

■ Therapeutic approaches

Due to the unique features of Glioblastoma (see below) it is not sufficient to target the tumour bulk as malignant cells will have already spread throughout the brain. Therapeutic approaches to target those cells are rather limited due to the blood-brain-barrier which prevents the free distribution of drugs throughout the brain. Hence novel approaches, drug combinations or treatment regiments are needed to over come these limitations. Such as the RIST therapy, which was developed in this clinic and is used in a compassionate use setting. [2]
Patho-clinical features of Glioblastoma

Glioblastoma only rarely metastasises outside the CNS but seems to not exist in a pre-invasive form. Understanding the underlying molecular mechanisms will help us to modulate the invasive nature of the Glioblastoma cells and transform it into a more localised, i.e. easier to treat disease. We have formulated the so-called Alcatraz Strategy that aims to prevent the interaction/communication of cancer cells with their environment. [3]

Taking these three aspects together gives us a clear aim of our research: By combining basic research and bidirectional translational research to improve our understanding how to a) target the unique features of Glioblastoma and b) adapt novel treatment approaches for their implementation in Glioblastoma treatment.

To answer these questions we have created a collection of ~300 case files with ~100 stored tumour samples and ~50 patient-derived cell populations.

References


Experimental Pediatric Oncology Section

Head: Prof. Dr. Christian Beltinger
Staff: Dr. Carmen Dorneburg, Dr. Célimène Galiger, Annika V. Goß, Nicole Heymann, Helgard Knauß, Astrid Laut, Lara M. Riehl, Ning Wei

In our focus “Molecular pathogenesis and diagnosis of neuroblastoma” we investigate the interaction of oncogenes with tumor suppressors in the genesis of neuroblastoma and we explore the feasibility of liquid biopsy in neuroblastoma patients. In our second focus ”Experimental therapy of neuroblastoma and acute lymphoblastic leukemia“ we develop novel preclinical strategies utilizing small molecules or oncolytic viruses against neuroblastoma and acute lymphoblastic leukemia (ALL).

Figure: A neuroblastoma that developed in a MYCN-transgenic mouse haploid for BIRC5 avidly takes up 18F-FDG (magenta) because of its strong Warburg effect. Shown is a MRI/PET fusion image.
■ **Focus “Molecular pathogenesis and diagnosis of neuroblastoma”**

Neuroblastoma is the most common extracranial solid tumor in childhood. The aggressiveness of neuroblastoma is determined by tumor-promoting and tumor-suppressive mechanisms that are inactivated or activated, respectively. We therefore investigate the interaction of oncogenes such as MYCN, BIRC5 and LDHA/B with dysfunctional tumor suppressors in the genesis, progression and aerobic glycolysis (Warburg effect) of neuroblastoma. To this end, we use cellular and molecular biology methods, transgenic and xenotransplant mouse models, and bioinformatic tools. We are translating the results of this preclinical work into establishing prognostic markers and liquid biopsy for neuroblastoma patients.

■ **Focus “Experimental therapy of neuroblastoma and acute lymphoblastic leukemia”**

Specificity and efficacy are major challenges in targeted tumor therapy. We develop novel approaches to address these challenges in neuroblastoma and acute lymphoblastic leukemia. To this end, we investigate small molecules that interfere specifically in signaling pathways crucial for neuroblastoma. In addition, we explore oncolytic measles virus against ALL. Our aim is to translate these novel preclinical therapies to the patient with neuroblastoma or ALL.

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**Leukemia**

Heads: apl. Prof. Dr. Lüder-Hinrich Meyer, Prof. Dr. Klaus-Michael Debatin
Staff: Dr. Stefanie Enzenmüller, Sevil Essig, Dr. Vera Münch, Alexandra Niedermayer, Dr. Felix Seyfried, Dr. Helen Sun, Dr. Julia Zinngrebe
Students: Elena Boldrin, Salih Demir, Malcom Meyer, Felix Stirnweiß

Among all pediatric cancers, acute lymphoblastic leukemia (ALL) is the most common malignant disease in childhood and adolescence. Over the past decades, substantial achievements have been made resulting in successful treatment of pediatric ALL and cure rates of more than 80%. Despite this success in pediatric oncology, therapy fails in about 20% of the patients leading to reoccurrence.

**Figure:** Central nervous system (CNS) leukemia modeled in the NOD/SCID/huALL system: (A) Massive meningeal infiltration with human ALL cells in NMRI scan analysis (left panel, white arrows indicate enlarged meninges) and immunohistochemistry (right panel, purple: human B-cell precursor cells, anti-human CD10 staining; and (B) absence of meningeal manifestation in a CNS negative ALL sample. [see Münch et al., Blood 2017; 130(5):643-654]
of the disease associated with clearly reduced prognosis and outcome. However, the majority of patients encountering relapse are not identified using the currently available risk markers and extramedullary leukemia manifestation outside the hematopoietic system as for example in the central nervous system remains a diagnostic and therapeutic challenge. Moreover, although generally well tolerated, anti-leukemia therapies bear the risk of late sequelae and side effects, in particular for intensified treatment in relapse situations. These problems and limitations clearly highlight the need for less toxic treatment modalities including directed therapies acting on identified targets and improved risk stratification.

In our Leukemia Research Group, the main interests focus on acute lymphoblastic leukemia (ALL). In our work, we want to better understand leukemia biology and to analyze and characterize molecular mechanisms of disease initiation, development and manifestation. Based on our findings, we aim to investigate and develop novel therapeutic approaches like evaluation of new risk markers and new therapeutic agents including preclinical validation in corresponding model systems. By combining comprehensive molecular and functional analyses, we characterize leukemia-specific biological mechanisms and try to identify possible starting points for new therapy strategies for leukemia. Moreover, we have established and refined a leukemia model that mimics the disease seen in patients thus allowing to investigate different aspects of disease biology but also evaluate new treatment modalities pre-clinically and have provided evidence for a good efficacy of several substances alone and in combination with conventional chemotherapy against different subgroups and manifestations of ALL.

**Immunoregulation and GvHD**

**Head:** apl. Prof. Dr. Gudrun Strauß  
**Staff:** Ingrid Knape, Dr. Yvonne Hüsecken, Malena Klingspor (medical student), Dr. Monika Kustermann, Silvia Muche, Tanja Reisser, Jasmin Scheurer, Linda Wolf

A functional immune system protects from disease development and autoimmunity. The immune response therefore requires a tight control to ensure that immune cells eliminate invading pathogens but do not attack the body’s own cells. Various molecular processes and cell types are involved in the regulation of the immune response.

The main focus of our research group deals with the regulation of the T cell immune response and the development of new treatment strategies for graft-versus-host disease (GvHD) prevention. GvHD is the major complication after allogeneic bone marrow transplantation leading to increased morbidity and mortality. T cells in the donor transplant, which are activated by antigens of the recipient, expand and subsequently attack and destroy recipient tissues thereby inducing GvHD. During the last years we have established several murine models of GvHD mimicking the human transplantation situation. Currently we are working on the following projects:

- **Modulation of the T cell immune response by death receptors**

Death receptors were initially characterized to induce apoptosis after ligation with their cognate death ligand. Nowadays, however, it is clear that death receptors have additional functions. We have recently investigated the influence of death receptor CD95 and TRAIL on T cell activation and define for the first time, that CD95 and TRAIL-receptors suppress T cell activation when stimulated by death ligands during T cell priming. This mechanism might contribute to immune evasion of viruses or other pathogens, which induce death ligand expression in target cells after infection.
Development of new treatment strategies for GvHD prevention

GvHD is characterized by recipient organ destruction induced by activated T cells. Since activated T cells strongly up-regulate death ligands we are exploring whether blocking of death ligand functions might serve as a possible treatment option in GvHD prevention. Destructive functions of activated T cells, however, can also be abrogated by suppressor cells. Myeloid-derived suppressor cells (MDSCs) are an immature population of myeloid cells inhibiting T cell activation, proliferation and function and are therefore under investigation for GvHD-prophylaxis. T cells do not represent a uniform population of cells but are subdivided in different subpopulations due to their phenotype and function. The impact of different T cell subpopulations especially Th9 cells on GvHD development is studied.

Function of myeloid-derived suppressor cells (MDSCs) in trauma

The immune response after traumatic injuries is predominated in the beginning by an overwhelming pro-inflammatory response of the innate immune system, followed by a suppression of the adaptive immunity leading to immunosuppression and an enhanced risk for all types of infections. At present, the impact of MDSCs on the course of disease and the immune response after trauma is not well defined. Using murine trauma models we determine the influence of trauma on the induction of MDSCs, define their potential to modulate T cell-mediated immune responses in order to clarify whether interference with MDSC development might be a therapeutic option after trauma.

Division of Paediatric Endocrinology and Diabetes

Head: Prof. Dr. Martin Wabitsch
Principal Investigators: Prof. Dr. Martin Wabitsch, Prof. Dr. Pamela Fischer-Posovszky, PD Dr. Christian Denzer, Dr. Stephanie Brandt, Dr. Julia von Schnurbein, Dr. Daniel Tews, Dr. Anja Moss
Staff: Dr. Patricia Cardenas de Bäuerle, Dr. Meike Dahlhaus, Dr. Friederike Denzer, Malaika Fuchs, Dr. Jan-Bernd Funcke, Daniel Halbgebauer, Dr. Gloria Herrmann, Alexandra Killian, Dr. Katja Kohlsdorf, Stephanie Laviani, Adriana Nunziata, Julian Roos, Dr. Heike Vollbach, Dr. Helmut Weyhreter

Our research areas include development and disturbances of the endocrine system, endocrine regulation of body weight and diabetes mellitus type 1 and type 2. The main focus of the research projects lays on diseases going along with alterations in adipose tissue mass and function such as obesity and lipo-dystrophies and their comorbidities. On the one hand (see Experimental Endocrinology and Metabolism Research) we aim to identify the underlying pathophysiology at the genetic, molecular, cellular, organ and systemic level. On the other hand, we are involved in clinical studies evaluating novel treatment options (see Externally Funded Research Projects and Studies).

Our objectives include not only the further development of a pure science of endocrinology
logy, but also the evolution of an applied science of endocrinology and the improvement of the medical art in endocrine domains. We believe that the promise of basic science is that tomorrow’s patients will be treated better than today’s.

- **Monogenic obesity**

Monogenic forms of early onset obesity are very rare. Severe early-onset obesity is often caused by genetic defects. Most of these genes are involved in the central nervous regulation of hunger and satiety. Herein, the leptin-melanocortin system plays a pivotal role. Patients with congenital leptin deficiency can be treated with a hormone replacement therapy with metre-leptin, a recombinant analogue of the human leptin. Leptin is a highly important hormone stimulating the MC4 pathway with pleiotropic functions mostly elicited via specific leptin receptors. Apart from regulating satiety, some of the most important aspects of leptin function include its influence on energy homeostasis, on glucose homeostasis, on the sympathetic nervous system and on immune function. Our department is one of a few centers worldwide offering leptin replacement therapy to patients. Furthermore, we have identified and treated the first known patients with severe early onset obesity due to a mutation in the leptin gene that renders the hormone biologically inactive (Wabitsch et al., New Engl J Med 2015). Our laboratory investigates the biological functions of leptin and aims to better understand the clinical picture of congenital leptin deficiency. Recently, the MC4R agonist Setmelanotide has been introduced as a new treatment option for patients with POMC and LPR deficiency (please see below - clinical study with Setmelanotide).

- **In vitro model systems to study human adipocyte biology**

In recent years we have developed model systems to study human adipocyte biology. We have established a cell line derived from an adipose tissue specimen of a patient with Simpson-Golabi-Behmel syndrome (SGBS). The cells are close to primary human adipocytes as they are neither transformed nor immortalized. SGBS adipocytes exhibit the typical characteristics of human white fat cells, including synthesis and storage of triglycerides and insulin sensitivity, as well as sensitivity to beta-adrenergic agents. Therefore, the cells represent a unique and versatile research tool for examining human adipose tissue biology. We share SGBS cells for scientific purposes. So far, the cells have been spread to more the 250 international research labs.

**Experimental Endocrinology and Metabolism Research (Heisenberg Professorship)**

- **Head:** Prof. Dr. Pamela Fischer-Posovszky
- **Staff:** Dr. Meike Dahlhaus, Jan-Bernd Funcke, Daniel Halbgebauer, Alexandra Killian, Adriana Nunziata, Julian Roos, Dr. Daniel Tews
- **Students:** Elena Brenner, Taner Pula

Obesity is a worldwide epidemic. The excessive accumulation of adipose tissue leads to the development of severe comorbidities such as insulin resistance, type 2 diabetes mellitus, hepatic steatosis, cardiovascular diseases including hypertension and atherosclerosis, and an increased risk of developing certain types of cancer. Conventional therapy concepts involving e.g. diet, physical exercise, or behavior therapy often fail. Thus, there is an urgent need to develop innovative pharmacological treatment strategies. In our group we aim to understand the physiology and pathophysiology of adipose tissue.
Death receptors in adipose tissue

Adipose tissue is a dynamic organ with ~10% of fat cells being renewed annually. Our group investigates the role of death receptors in this remodeling process.

We found out that preadipocytes and adipocytes express death receptors, among them CD95, TNF receptors, and TRAIL receptors. Interestingly, both cell types are protected from apoptosis induced by their respective ligands. Apoptosis of adipocytes can only be induced under certain conditions, e.g. by inhibition of protein biosynthesis (Fischer-Posovszky et al., Endocrinology 2004).

In our current projects we study non-apoptotic function of death receptors in adipose tissue. We have elucidated that TRAIL stimulates the proliferation of preadipocytes and inhibits their adipogenic differentiation (Funcke et al., FASEB J 2015; Zoller et al., Cell Death Dis 2016).

MicroRNAs in adipose tissue

MicroRNAs (miRNAs) are small, 18-25 nucleotide long, non-coding RNA molecules. They are central regulators of gene expression and influence a variety of biological processes including cellular differentiation and metabolism.

Obese adipose tissue is characterized by pathological alterations such as hypertrophy of adipocytes, inflammation, hypoxia, and fibrosis. We showed that miRNAs are differentially regulated by inflammatory stimuli in adipocytes (Roos et al., Sci Rep 2016). We now aim at identifying the function of specific miRNAs. miR-146a, for example, was identified as a negative regulator of the inflammatory response in adipocytes (Roos et al., Sci Rep 2016).

miRNAs can be released to the circulation. We also seek to find out if these small RNA molecules might constitute novel biomarkers of adipose tissue health.

Brown adipose tissue

The discovery of active brown adipose tissue in adult humans and its negative association with fat mass and body weight gave rise to the idea, that this special tissue could be utilized for the treatment of obesity and metabolic disease.

Brown adipocytes are characterized by the expression of uncoupling protein-1 (UCP1). This mitochondrial protein is capable of uncoupling cellular respiration from ATP synthesis. The proton gradient, which is built up by the electron transport chain is not used for the production of ATP. Instead, energy is dissipated as heat. UCP1 is activated by cold or β-adrenergic agents, which stimulate lipolysis and result in the metabolism of free fatty acids. Therefore, brown adipocytes can consume stored energy. White adipocytes do not express UCP1 and are thus not capable of thermogenesis. They are responsible for the storage of excess energy, which can be mobilized as needed. A third, intermediate phenotype of fat cells was named beige adipocyte. Beige adipocytes express UCP1 and are thermogenic. They can form within white adipose tissue depots, e.g. upon prolonged cold exposure, in a process called “browning”.

Our laboratory investigates white and beige/brown adipose tissue in humans. From surgical operations in the neck region we collected paired samples of subcutaneous, white adipose tissue and brown adipose tissue from the deep neck region (Tews et al., Mol Cell Endocrinol 2014). Progenitor cells isolated from both depots showed a distinct gene expression profile. We currently study whether the differentially expressed genes play a role in white or brown adipogenesis.
Non-malignant hematological diseases

Head: apl. Prof. Dr. Holger Cario
Cooperations: Molecular Diagnostics and Therapy Group at IKT Ulm (Dr. K. Schwarz), European Congenital Erythrocytosis Consortium (ECE) and MPN&MPNr Euronet (COST)

■ Congenital erythrocytoses

In patients without underlying cardiac or pulmonary diseases, erythrocytoses are a very rare, heterogenic group of diseases. There is only few systematically collected data on basic principles, presentation and therapy of these etiologically in many cases unclear disease patterns, neither on polycythemia vera in pediatric patients. On these grounds, a register for these diseases was established in Germany, in which patients from other European countries are included as well. It now forms the basis for a European register (www.erythrocytosis.org).

In the recent years we identified several hitherto unknown mutations which, occasionally in connection with other genetic or epigenetic alterations, contribute to primary and secondary congenital erythrocytosis. These efforts are currently continued with a focus on secondary congenital erythrocytosis. In cooperation with the MPN&MPNr Euronet (B. Gardie, Nantes), there are furthermore functional analyses of the potential pathogenetic role of the identified mutations.

■ Hemoglobin diseases

The department is a center for the treatment of patients with hemoglobin disorders, in particular thalassemia and sickle-cell disease. It has laid important foundations for clinical scientific and epidemiological works on thalassemia and sickle-cell disease in Germany. The German Society for Pediatric Oncology and Haematology established a consortium coordinating a new register study on sickle-cell disease in which Ulm is participating.

Immunodeficiency and Stem Cell Transplantation

Head: apl. Prof. Dr. Ansgar Schulz
Investigators: PD Dr. Manfred Höning, Dr. Catharina Schütz, Dr. Eva Jacobsen, Andrea Hänsler

■ Primary Immunodeficiencies

Through our long lasting experience with diagnosis and therapy of primary immunodeficiencies – particularly stem cell transplantsations in severe combined immunodeficiencies (SCID) – a unique cohort of patients has grown. Our scientific points of interest are 1. Individualized therapy through an as exact as possible characterization of the clinical phenotype; 2. Identification of the underlying genetic causes of the disease; 3. Long-term course of disease after successful stem cell transplantation under consideration of non-immunological symptoms of the disease. Our work in all three areas cumulated in successful publications.

Our group closely cooperates with Dr. Schwarz (Molecular Diagnostics and Therapy at IKT Ulm). We are part of a BMBF-funded nationwide research network (PID-NET) on phenotypic and genetic characterization of inborn immunodeficiencies. Currently, we are collecting data from worldwide sources on clinical presentation and therapy of patients with reticular dysgenesis, a rare subgroup of the severe combined immunodeficiency and granulopenia.
Osteopetrosis

The Department of Pediatrics and Adolescent Medicine of Ulm University has long standing experience with diagnosis and therapy of the various forms of osteopetrosis. Our group contributed to the identification of additional genetic variants. In addition, we were able to further optimize various therapeutic approaches in the field of hematopoietic stem cell transplantation. Our hospital is now one of the leading contacts in the area of osteopetrosis.

In order to further pursue the goal of improving diagnosis and therapy of this rare disease, a network of basic scientists and clinicians from many European countries was established by the E-RARE initiative of the European Union. The following goals of the sub-project from Ulm were reached and are now widened: a) the registration of European patients with infantile osteopetrosis in a central register and b) the development of recommendations for diagnosis, therapy and clinical monitoring of patients with osteopetrosis.

Neonatology and Pediatric Intensive Care

Acting Head: Dr. Wolfgang Lindner

Clinical Research

The Division of Neonatology is actively participating in scientific clinical studies to improve patient care. We participated in multicenter studies on the effects of automated adjustment of the inspired oxygen on fluctuations of oxygen saturation together with University Hospital Tübingen (Investigators: Dr. Mendler and Dr. Essers).

Currently we participate in two large international studies (SAIL-Trial, Premod-Trial) with special focus on delivery room care (investigators: Dr. Essers and Dr. Mendler). Furthermore, we are working together with Stephan Medizintechnik GmbH with the aim to improve non-invasive respiratory support of newborns and participate in the German Neonatal Network (GNN, investigators: Dr. Essers and Dr. Schiefele). These studies are funded by the Federal Ministry of Economic Affairs and Energy.

Experimental Neonatology

In close collaboration with several physicians and guest scientists, we perform studies with laboratory animals on resuscitation of newborns. The animal lab is supervised by Dr. Mendler.
who conducts studies on resuscitation after circulatory collapse due to asphyxia together with his team of physicians and students. One focus is on the respiratory support during cardiac massage. These studies are funded by the German Research Foundation (DFG).

**Pediatric Gastroenterology**

**Head:** PD Dr. Carsten Posovszky  
**Staff:** Kirsten Lang, MD; Lena Wölfle, MD; Susanne Stephan, MD; Doris Gülke, MD; Andrea Kresz, MD; Monika Kriechbaum, dietician; Sigrid Räkel-Rehner, dietician; Maria Zernickel, study nurse  
**Funding:** German Research Foundation (DFG), industry

The Division of Pediatric Gastroenterology, Hepatology and Nutrition advances the treatment of pediatric gastrointestinal and liver diseases through the coordinated efforts of its patient care, research and educational activities. As part of an academic medical centre, researchers and clinicians work continually together to improve the standard of care. Our research includes both basic and clinical investigations and involves other disciplines. Exploring the molecular and genetic origin of chronic gastrointestinal diseases, transform pathogenesis findings into most advanced diagnostics, drug therapies and procedures available today. There are ongoing multicentre interventional trials for children with chronic functional abdominal pain, chronic inflammatory bowel disease and paediatric endoscopy.

**Clinical Research**

Our research interests include single- and multi-center clinical studies in inflammatory bowel disease, vaccination of immunosuppressed patients, pediatric endoscopy and pediatric functional abdominal pain.

Currently we participate in several prospective randomized trials and long-term-safety observations regarding therapeutic agents in inflammatory bowel disease. Our group is a member of the German inflammatory bowel disease register (CEDATA). A randomized controlled trial evaluating carbon dioxide insufflation during colonoscopy was performed at our center. Currently, we recruit patients for a randomized controlled trial evaluating safety and efficacy of a new bowel cleansing preparation in pediatric patients (Easykid). We also initiated multi-center observational studies on life vaccination in immunosuppressed patients founded by the German Crohn and Colitis Organization (DCCV). Furthermore, we have just recently finished a multi-center study funded by the German Research Foundation (DFG), which aimed to improve the treatment of children with functional abdominal pain (STOP-FAP).

Mislocated PAS-positive granula in the intestinal epithelium of a Patient with FHL Typ5 due to STXBP2 Mutation on the right.
**Experimental Gastroenterology**

Our basic research focuses on the cellular and molecular pathogenesis of congenital enteropathies and inflammatory bowel diseases. We contributed to the identification of the gastrointestinal pathomechanisms involved in Autoimmune-Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED) and Familial Hemophagocytic Lymphohistiocytosis (FHL) Type 5.

In order to further pursue the goal of improving the genetic and pathophysiological understanding of congenital gastrointestinal diseases we investigate cellular trafficking and inflammatory pathways in the gut. We perform these studies in a network of European collaborators.

**Pediatric Cardiology**

**Head:** apl. Prof. Dr. Christian Apitz  
**Investigators:** Dr. Peter Bride, cand. med. Miriam Heinzelmann, Dr. Michael Kaestner, cand. med. Verena Kiesler, Dr. Johannes Krämer, Dr. Fabian von Scheidt, Dr. Jannos Siaplaouras

The research focus of the Division of Pediatric Cardiology is on diagnosis and treatment of pulmonary hypertension and heart failure. In this regard, we are actively participating in scientific national and international clinical studies to investigate innovative therapies for the care of patients with pulmonary hypertension (Riociguat, Tadalafil) and heart failure (Sacubitril/Valsartan). To collect data on etiology, prevalence and treatment strategies, we participate in several national and international registries for pulmonary hypertension and heart failure/myocarditis (CompERA, TOPP, Mykke).

A further research topic of interest of the Division of Pediatric Cardiology is modern imaging techniques for the early detection of myocardial dysfunction potentially resulting in heart failure due to different causes. These studies are funded by a research grant of the German Association for Pediatric Cardiology. In addition, we are participating in an international multicenter study to investigate factors leading to the development of protein-losing enteropathy, a life-threatening complication in patients with failing single-ventricle hemodynamics, as for example with the hypoplastic left heart syndrome.

Another thematic focus of the Division of Pediatric Cardiology is the systematic assessment of physical activity in children and adolescents with congenital heart disease in collaboration with the German Competence Network Congenital Heart Defects and the Karlsruhe Institute of Technology. We are further evaluating home based training programs to allow patients with congenital heart disease active sports participation.

**DNA Damage Response in Human Lymphocytes**

**Head:** Dr. Kerstin Felgentreff  
**Staff:** Jasmin Sprissler, Dilek Dayanakli  
**Cooperation:** Institute for Clinical Transfusion Medicine and Immunogenetics (IKT) Ulm, Dr. K. Schwarz Group  
**Funding:** German Research Foundation (DFG), Else-Kroener-Fresenius Foundation

DNA damage occurs ubiquitously in every cell and is triggered by endogenous factors of metabolism, or exogenous influences such as ionizing radiation or intercalating chemical drugs. The cellular integrity relies on a complex repair system that ensures immediate sensing and efficient
repair to protect the DNA from any persisting damage, known as DNA damage response. If this system fails, apoptosis, senescence, or introduction of chromosomal breaks and mutations potentially leading to neoplastic transformation are the consequences. Furthermore, DNA double strand breaks are physiologically induced, such as in the process of V(DJ) recombination in lymphocyte development for generation of diversified T cell and immunoglobulin receptors. Recombination activating genes RAG1 and RAG2 target specific signal sequences to cleave adjacent DNA. Subsequently, DNA ends are processed and joined by factors of the non-homologous end-joining (NHEJ) DNA repair pathway.

■ Analysis of DNA Damage Response

Genetic defects in genes coding for DNA repair proteins can cause various immunodeficiencies due to impaired lymphocyte development and survival. The only treatment option for many of these diseases is the allogeneic hematopoietic stem cell transplantation, although associated with increased toxicity to conditioning regimens. Early diagnosis of increased radio- and chemosensitivity, for example in severe combined immunodeficiency, has a tremendous impact on treatment decisions regarding use of chemotherapy and diagnostic medical radiation.

We are working on diagnostic assays to rule out radio- and chemosensitivity that allows an early diagnosis of DNA repair deficiencies using biomarkers on peripheral blood mononuclear cells.

■ Recombination-induced DNA damage response

Although transient, RAG-induced DNA double strand breaks launch a DNA damage response that impacts on transcriptional regulation for cellular-processes beyond canonical DNA repair.

There is evidence in mice that RAG proteins are already expressed in early lymphoid progenitors and also target sequences in developing NK cells with important DDR-related effects on maturation, cytotoxic function and cellular fitness. We are using induced pluripotent stem cells (iPSC) as a platform to study DNA damage response after RAG-cleavage in lymphocyte differentiation.
Externally Funded Research Projects and Studies

Consortium “Adolescents with Extreme Obesity”
(Competence Network Obesity, CNO)

Speaker: Prof. Dr. Martin Wabitsch
Funding: Federal Ministry for Education and Research (BMBF)
Duration: 2012 - 2018
Partners: University Children’s Hospitals at Essen, Witten-Herdecke, Berlin and Leipzig; Institute for Epidemiology and Medical Biometry of Ulm University, Helmholtz Center Munich
Registry IDs: DRKS00004172, DRKS00004198, DRKS00004195, DRKS00009437, DRKS00004196, DRKS00004197 (Deutsches Register Klin. Studien)

Extremely obese adolescents are at a strongly elevated risk of early death, somatic comorbidities, psychiatric disorders, and social isolation, including unemployment, due to both functional impairment and stigmatization. Despite the dire implications of extreme obesity in adolescents and the frequently overt (e.g. orthopaedic disorders) and non-overt (e.g. hypertension) comorbidity, these adolescents are difficult to reach and treat in medical terms. Thus, only a small percentage actively seeks treatment.

The underlying reasons are poorly understood and may presumably be attributed to the young age, a predominantly low educational and socioeconomic status, as well as to functional impairment due to inactivity and psychiatric comorbidity. Unsuccessful attempts to lose weight on their own and/or within the medical system may have led to frustration with respect to their behaviour in seeking treatment.

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

Collaborative Research Center SFB 1074: Experimental Models and Clinical Translation in Leukemia

Speaker: Prof. Dr. Hartmut Döhner, Department of Internal Medicine III
Vice Speaker: Prof. Dr. Klaus-Michael Debatin
Funding: German Research Foundation (DFG)
Duration: 2016 - 2020 (second funding period)
Partners: Additional Departments and Institutes of Ulm University
Subproject *Genomic and signalomic characterization of pre- and post-therapy ALL modeled in vivo*

**Investigator:** apl. Prof. Dr. Lüder H. Meyer, Prof. Dr. Klaus-Michael Debatin

Despite the great success in treating pediatric acute lymphoblastic leukemia (ALL) with elaborated risk-stratifying protocols, resulting in cure rates of more than 80%, 20% of the patients will relapse resulting mostly in poor outcome. The majority of relapses occurs in the standard-risk group.

Over the last years, molecular and functional analyses of ALL have identified mechanisms and characteristics of leukemia biology such as activating mutations, dysregulated pathways, and clonal selection at relapse opening the avenue for pathway-directed therapies. However, translational studies in patient-derived ALL are limited by the restricted availability of cells and the inability to culture primary ALL cells in vitro. Thus, preclinical xenograft models, using primary patient-derived ALL cells transplanted into immunodeficient mice, are used to overcome these restrictions.

We have established a NOD/SCID/hu-ALL xenograft model for pediatric ALL and have built up a large biobank of ALL xenografts derived from more than 130 individual pediatric ALL patients. In this model, we have identified a specific gene expression signature, which characterizes ALL samples with rapid engraftment, i.e., a short-time to leukemia development (TTLshort) and poor prognosis. This TTLshort phenotype is characterized by a hyperactivated mTOR signaling pathway and in vivo treatment using combinations of mTOR-directed therapies with chemotherapy was highly effective. By genomic profiling, we have characterized mutation frequencies upon repeated transplantation and diagnostic ALL samples and obtained miRNA signatures. Using candidate genes of the TTL signature, we identified novel targets by RNA interference and obtained first evidence for an anti-CD70-directed immunotherapy as novel treatment strategy in B-cell precursor ALL. Lastly, we identified defective apoptosis signaling as an additional feature associated with the TTL signature which could be restored by Smac-mimetics such as BV6.

Taking further advantage of this xenograft model, we will perform an in-depth analysis with a particular focus on genomic alterations, functional status and clonal evolution of ALL between diagnosis and relapse. To this aim, we will characterize genomic signatures in primary ALL and at the time of relapse occurring after conventional short term treatment in the NOD/SCID/hu-ALL system. This will include clonal analysis to address issues of heterogeneity and drug resistance of individual clones. Furthermore, this analysis will be extended to paired samples from patients analyzed at diagnosis and relapse. The genomic analysis will be complemented by multicolor-phosphoflow and phosphoproteomic analyses of individual leukemia cells. To this aim, we will also make use of the newly established CyTOF technology, allowing multimarker analysis of surface and cytoplasmic molecules at the single cell level. Furthermore, we will analyze sensitivity and resistance for targeting of specific pathways involved in differentiation, survival and apoptosis such as PI3K, mTOR, pre-B-cell receptor, B-cell receptor, IL7 receptor, Bcl-2 and IAP. This approach can also be used for novel compound screening in the appropriate setting.

Taken together, given the fact that we have established one of the largest cohorts of pediatric ALL in the NOD/SCID/hu-ALL model, we expect that our studies will not only give a more detailed insight into leukemia biology and possible prognostic markers, but will also help identifying rational targets for novel therapeutic interventions.
Collaborative Research Center SFB 1149: Danger Response, Disturbance Factors and Regenerative Potential after Acute Trauma

**Speaker:** Prof. Dr. Florian Gebhard (Department of Orthopaedic Trauma, Hand, Plastic, and Reconstruction Surgery)

**Funding:** German Research Foundation (DFG)

**Duration:** 2015 - 2018 (first funding period; continuation granted)

**Partners:** Additional Departments and Institutes of Ulm University

### Subproject Role of myeloid-derived suppressor cells (MDSCs) in trauma

**Investigator:** apl. Prof. Dr. Gudrun Strauß

The clinical course after trauma depends on the balance or imbalance of pro- and anti-inflammatory responses. While predominance of a pro-inflammatory response leads to “systemic inflammatory response syndrome” (SIRS) and overwhelming immune reactions, inhibition of the immune response induces the “compensatory anti-inflammatory response syndrome” (CARS) connected with immunosuppression and an enhanced risk for all types of infections. Traumatic injuries are associated with the release of pro-inflammatory factors such as TNF-α, IL-6 or glucocorticoids, which shape the immune response. Several types of inflammation such as tumors, autoimmunity, and bacterial infections are known to induce a population of immature myeloid cells, which suppress T cell-mediated immune responses such as T cell activation, proliferation, and cytotoxicity. These heterogeneous populations of immature myeloid cells are defined as myeloid-derived suppressor cells (MDSCs) and are characterised by the co-expression of surface molecules CD11b and Gr-1. At present, the impact of MDSCs on the course of disease and the innate and adaptive immune responses after traumatic injuries are not well defined. A few studies point to a beneficial effect of MDSC appearance for the injured host, however, their precise effects on innate and cellular immunity are unclear. Therefore, we will use different trauma models – preferentially blunt chest trauma and blunt chest trauma in combination with femur osteotomy – to define the kinetics of MDSC induction after injury and determine their influence on innate immunity and T cell functions. Using MDSC-depleting antibodies or the injection of in vitro-generated MDSCs will show at which time point after trauma, MDSCs interfere with the trauma-induced immune response and whether induction of MDSCs is detrimental or advantageous for the injured host. A major focus of the studies will be the modulation of T cell functions by trauma-induced MDSCs. Immune suppression and susceptibility for opportunistic infections after trauma is often associated with a skewing towards Th2 immunity and the loss of Th1-specific cytotoxicity. Whether and how MDSCs influence the Th1/Th2 balance after traumatic injuries will be analysed. Since pro-inflammatory factors such IL-6 and glucocorticoids are strongly induced after blunt chest trauma and are known to be required for the expansion and maturation of MDSCs, we will delineate the role of IL-6 and GC for MDSCs induction and T cell immune responses. Analysis of MDSCs induction and function and their influence on T cell-mediated immune responses in other trauma models will further clarify whether MDSCs have a general impact on the course of traumatic injuries and how they influence SIRS and CARS. The anticipated results will define the role of MDSCs after traumatic injury and might help to clarify whether interference with MDSC development is a possible therapeutic option after trauma induction.

### Subproject Role of severe obesity in healing of muscle injuries

**Investigators:** Prof. Dr. Uwe Knippschild (Department of General and Visceral Surgery), Prof. Dr. Martin Wabitsch
In obesity, adipose tissue functions are dysregulated leading to changes in the release of growth factors, 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 homeostasis, inflammation, angiogenesis, haemostasis, and blood pressure. In addition, the ectopic lipid accumulation in organs and tissues can lead to severe co-morbidities including heart disease, diabetes, metabolic syndrome, hypertension, sleep apnoea, and cancer. Furthermore, there is increasing evidence that obesity impairs tissue regeneration processes after trauma. For example, obesity negatively affects regeneration of skeletal muscle injuries, yet the underlying mechanisms have not been elucidated. Muscle regeneration can be divided into an initial response, i.e. the peak inflammation and degenerative response, and the structural and functional recovery phase. It is a highly synchronised process demanding the timely coordinated activation of different cellular responses by many different signalling molecules. There is evidence that toxic lipid metabolites and pro-inflammatory adipocytokines and chemokines as well as leptin and insulin resistance impair these processes, especially muscle satellite activation and functions, finally resulting in decreased regenerative ability. The aim of our project 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 on muscle regeneration, and (iii) how changes in signal transduction pathways affect satellite cell physiology. The results of our project will lead to the identification of new obesity-related factors with prognostic and therapeutic relevance in regard to muscle regeneration after injury.

**Boehringer Ingelheim Ulm University BioCenter (BIU)**

**Speaker:** Prof. Dr. Klaus-Michael Debatin (on behalf of the Medical Faculty)  
**Funding:** State of Baden-Württemberg, Boehringer Ingelheim, Medical Faculty  
**Duration:** 2016 - 2019 (second funding period)  
**Partners:** Groups from Ulm University and from Boehringer Ingelheim, Biberach  
**Topics:** Cardio-metabolic and lung diseases, neuropsychiatric diseases and immunomodulation

- **Subproject Role of secreted factors for white and brown adipocyte differentiation**
  
  **Investigators:** Dr. Daniel Tews, Prof. Dr. Pamela Fischer-Posovszky, Dr. Bradford Hamilton (Boehringer Ingelheim Pharma GmbH & Co. KG, Cardiometabolic Diseases Research)

In this project, we concentrate on preadipocyte-secreted factors and their impact on brown adipocyte differentiation using our state-of-the-art model of ex vivo differentiated primary human deep neck preadipocytes.

Secreted factors and their respective receptors are promising targets to develop novel drugs for obesity treatment by promoting brown adipocyte differentiation. We hypothesize that the progenitor pool within the adipose tissue releases factors, which modulate either white or brown adipocyte differentiation in an auto-/paracrine manner.

UCP1 (UCP1/DAPI) immunostaining of differentiated adipocytes from brown adipocyte progenitor cells ex vivo.
Subproject Influence of inflammation on the differentiation and function of MDSCs and T cell-mediated immune responses

Investigators: apl. Prof. Dr. Gudrun Strauß, Prof. Dr. Klaus-Michael Debatin

This project aims to clarify how the disease-specific inflammatory environment influences the outcome of a MDSC therapy. By using three different murine disease models (graft-versus-host disease (GvHD), adipositas and trauma) the differentiation and immunosuppressive capacity of MDSCs and their subsequent effect on the adaptive immune response will be determined. This work will help to estimate the therapeutic success of MDSC treatment dependent on the disease entity.

RECOMB: Stem-cell based gene therapy for recombination deficient SCID

Coordinator: Prof. Dr. Frank Staal, Leiden, The Netherlands
Our Investigator: apl. Prof. Dr. Ansgar Schulz
Funding: European Union – Horizon 2020
Duration: 2018 - 2022
Partners: 17 partners in Europe and Israel

Recomb is a multi-stakeholder research consortium aiming to create a novel treatment for severe combined immunodeficiency (SCID) by conducting clinical trials using gene therapy for one of the most common type of SCID: RAG-SCID. The consortium, started in 2018, brings together clinical and research professionals from 16 European and 1 Israeli institutes with expertise in the management of primary immunodeficiencies, such as SCID. The project received funding from the European Union Horizon 2020 programme.

SCID comprises a group of rare diseases in which cells in the adaptive immune system fail to develop properly. The specific SCID phenotype depends on the underlying genetic defect, and more than 20 SCID-associated genes have been identified to date. SCID affects around 1:35,000 infants, with approximately 145 affected babies born each year in the EU.

These infants are born without a functional immune system, thus typically experience a wide range of serious, eventually life-threatening infections, including pneumonia, meningitis, and sepsis, and die within the first year of life unless effective treatment is given.

Source: Recomb leaflet; www.recomb.eu

International Registry for the Therapy of Patients with Severe Combined ImmunoDeficiency, SCID

Speaker: PD Dr. Manfred Hönig
Funding: Deutsche Kinderkrebsstiftung
Duration: 2018 - 2020
Partners: University Children’s Hospitals in Munich (LMU), Vienna, Freiburg, Zürich, Leipzig and Hannover

The term “Severe combined Immunodeficiency, SCID” describes a heterogeneous group of rare diseases which are clinically defined by the lack of specific immune function. Without cellular therapies such as allogeneic Hematopoetic Stem Cell Transplantation (HSCT) or gene therapy, affected children die within their first year of life from recurrent and abnormal and
severe infections. As patients are treated in multiple centers all over Austria, Switzerland and Germany it is crucial to gather data in a central registry for scientific evaluation.

The intention of this international registry is to collect prospective data on all patients treated in participating countries with the diagnosis of Severe Combined Immunodeficiency (SCID). Information on the clinical presentation, immunophenotype, genotype, transplantation and follow up (cGvHD, chimerism, immunological reconstitution, frequency of infections and quality of life) will be gathered in a central database. With the inclusion in the registry and after transplantation patient samples will be cryopreserved in a biobank for future scientific projects. Counselling on therapeutic options and strategies is offered by the members of the board.

Scientific work up of registry data, clinical counselling and accompanying studies with the samples stored in the biobank will contribute to improving the standard of medical care for patients with SCID.

**Preclinical Comprehensive Cancer Center (PCCC)**

**Coordinator:** Prof. Dr. Hellmut Augustin, German Cancer Research Center, Heidelberg  
**Our Investigators:** Prof. Dr. Klaus-Michael Debatin, apl. Prof. Dr. Lüder H. Meyer, Dr. Stefanie Enzenmüller  
**Funding:** Helmholtz Association  
**Duration:** 2013 - 2016  
**Partners:** Additional Departments and Institutes of Ulm University; Helmholtz Centers DFKZ, HMGU, MDC; EMBL, Max-Planck Institute for Brain Research, and the Universities of Heidelberg, Munich (TU) and Cologne

The availability of advanced preclinical tumor models has emerged as one of the most rate-limiting factors for both, the advancement of basic tumor biology and translational oncology research. Therefore, the Helmholtz Association has established the Helmholtz Alliance Preclinical Comprehensive Cancer Center (PCCC) as a nationwide network for the development and validation of established and novel preclinical cancer models of superior quality, which truly mimic the natural course of human tumor initiation, growth and metastasis. Our mission is to translate discoveries into the clinic: from bench to bedside. Focusing on key issues of contemporary oncology research, such concerted effort holds great prospect to revolutionize current cancer research.

Source: Helmholtz Association; www.dkfz.de

**German Mass Cytometry Network**

**Speaker:** Dr. Henrik Mei, German Rheumatism Research Centre Berlin  
**Our Investigator:** PD Dr. Manfred Hönig (on behalf of the Cytometry Core Facility)  
**Funding:** German Research Foundation (DFG)  
**Duration:** 2017 - 2020  
**Partners:** DRFZ, Deutsches Rheumaforschungszentrum Berlin; CRTD, Center for Regenerative Therapies TU Dresden; BCRT, Berlin-Brandenburger Centrum für Regenerative Therapien

The detection of fluorochromes as markers of specific antibodies in flow cytometry is currently limited to 12-16 colors due to technical reasons. This limitation can be overcome by the use
of metal tags conjugated to specific antibodies in single cell mass cytometry. With this technology, currently more than 35 epitopes can be stained on a single cell. A detailed characterization of cell surface proteins combined with the staining of intracellular (phosphorylated) proteins opens new fields and perspectives for phenotypic and functional studies in hematology, oncology and immunology.

The establishment of staining protocols for intra- and extracellular antigens and the management of the huge amount of data pose major challenges in the use of this emerging technology.

To accelerate and facilitate the use of Mass Cytometry five centers gathered in a national network to exchange experience, data and protocols. The Core Facility Cytometry of the Medical Faculty of Ulm University was a founding member of this network and started the service in Mass Cytometry in March 2017.

**Identification and enrichment of beige/brown adipocyte progenitors from white adipose tissue for the generation of functional brown fat in humans**

**Investigator:** Prof. Dr. Pamela Fischer-Posovszky  
**Funding:** German Research Foundation (DFG)  
**Duration:** 2016 - 2020

The existence of functional 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 became an attractive pharmacological target for the treatment of overweight and obesity. Besides white and brown adipocytes a third adipocyte type has been recently described – the so-called “beige” adipocyte. In mice, this cell type emerges under certain circumstances within the WAT depot. 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.

Our group demonstrated recently that human progenitor cells of white and brown adipocytes have distinct gene expression signatures. Among the differentially expressed genes were many surface proteins, which could potentially be used to enrich brown adipocytes.

The fundamental hypothesis within this project is that specific progenitor cells, which are able to differentiate into functional brown or beige adipocytes reside in the stromal-vascular fraction of white adipose tissue depots. Specific aims are: 1. We want to identify surface markers of human white and beige/brown adipocyte progenitors. 2. We want to use these markers to enrich beige/brown adipocyte progenitor cells from white adipose tissue. 3. We will investigate if the identified markers play a causal role for the generation of beige/brown adipocytes. 4. Taking advantage of transplantation experiments, we want to test if progenitor cells enriched from WAT which display a beige/brown gene signature in vitro can give rise to functional beige/brown adipocyte tissue in vivo. In mice, transplantation of BAT can prevent or revert diet-induced obesity and its associated comorbidities. Our vision is to develop such a strategy for humans. The planned experiments provide a scientific basis for this approach.
Healthy Fat for a Healthy Life - Targeting Adipocyte Adipose Tissue Function to Maintain and Improve Systemic Metabolism (Heisenberg Professorship)

Investigator: Prof. Dr. Pamela Fischer-Posovszky  
Funding: German Research Foundation (DFG)  
Duration: since 2017

Overweight and obesity have reached epidemic proportions worldwide. The excessive accumulation of white adipose tissue leads to the development of severe comorbidities including insulin resistance, type 2 diabetes mellitus, hepatic steatosis, cardiovascular problems, and to an increased risk of developing certain types of cancer. Conventional therapy such as dietary and exercise intervention often fail in the long run. Therefore, there is an urgent need to develop innovative treatment strategies.

This research project aims at developing strategies to maintain and/or restore adipose tissue health to provide a basis for systemic metabolic health.

Role of microRNAs for obesity-associated adipose tissue inflammation

Investigator: Prof. Dr. Pamela Fischer-Posovszky  
Funding: Baden-Württemberg Stiftung  
Duration: 2015 - 2018

Obesity leads to an accumulation of white adipose tissue. Obese adipose tissue is characterized by local inflammation, hypoxia, and fibrosis. These pathological alterations play a causative role in the pathogenesis in associated diseases. We hypothesize that microRNAs play an important role in obesity-associated inflammation of white adipose tissue. This project aimed at the identification of microRNAs involved in inflammatory processes in adipose tissue, the elucidation of their functional role, and their suitability as biomarker to estimate adipose tissue inflammation.

The role of transcription factors in human brown adipocyte development

Investigator: Dr. Daniel Tews (Division of Pediatric Endocrinology and Diabetes)  
Funding: German Research Foundation (DFG)  
Duration: 2018 - 2020  
Partners: Picower Institute for Learning and Memory, MIT, Cambridge, USA  
(Prof. Elly Nedivi)  
Department of Nuclear Medicine, Ulm University Medical Center  
(Prof. Ambros Beer)

Brown adipose tissue (BAT) is the key thermogenic tissue in hibernating and newborn animals and has recently been shown to be present and active in adult humans. It is involved in body weight regulation and is currently discussed as a promising therapeutic tool to combat obesity and insulin resistance in humans. Upon cold exposure or pharmacological treatment, brown-like adipocytes can also emerge in white adipose tissue (WAT), representing another phenotype of adipocytes differentiating from a certain subtype of progenitor cells. Using gene array analyses, we recently identified a list of transcription factors differentially expressed in progenitor cells isolated from human brown and white adipose tissue. In this project, we aim
to elucidate the function of these factors concerning brown adipocyte identity using gain-and loss of function experiments and functional assays. Knock-out mouse models are used to assess the role of the respective genes on the systemic level. Characterization of these genes will thus provide potential targets for therapeutic intervention of obesity.

**An Open Label, 1-Year Trial, including a Double-Blind Placebo-Controlled Withdrawal Period, of Setmelanotide (RM-493), a Melanocortin 4 Receptor (MC4R) Agonist, in Leptin Receptor (LEPR) Deficiency Obesity due to Bi-Allelic Loss-of-Function LEPR Genetic Mutation**

**Investigator:** Prof. Dr. Martin Wabitsch  
**Sponsor:** Rhythm Pharmaceuticals, Boston, USA  
**Duration:** 2017 - 2020  
**Partners:** Dr. Erica van den Akker (Obesity Center CGG, Rotterdam), Prof. Dr. Sadaf Farooqi (University of Cambridge), Prof. Dr. Karine Clément (Sorbonne Université, Paris)  
**Trial ID:** RM-493-015

Patients with mutations in the leptin receptor (LEPR) gene suffer from severe hyperphagia and obesity caused by the lack of activation of the MC4 pathway, which prevents control of appetite and weight. LEPR deficiency represents a very rare genetic disorder of obesity. Unfortunately, these patients cannot benefit from treatment with metreleptin. The investigational medicinal product setmelanotide is undergoing clinical trials in patients with loss-of-function mutations in the LEPR gene. Representing a new-generation melanocortin-4 receptor (MC4R) agonist, setmelanotide is thought to activate the melanocortin 4 receptor (MC4R), part of a key biological pathway in humans that regulates appetite, caloric intake and energy expenditure. Setmelanotide is expected to become a potential replacement therapy that may restore lost activity in the MC4 pathway, resulting in substantial reductions in hyperphagia and body weight, re-establishing weight and appetite control. Our Division of Paediatric Endocrinology and Diabetes is one of four study centres in Europe enrolling patients in a Phase 3 clinical trial evaluating long-term (one year) safety and efficacy of setmelanotide in LEPR deficiency obesity.
A randomised, multinational, active-controlled, open-labelled, dose-finding, double-blinded, parallel group trial investigating efficacy and safety of once-weekly NNC0195-0092 treatment compared to daily growth hormone treatment (Norditropin® FlexPro®) in growth hormone treatment naïve pre-pubertal children with growth hormone deficiency REAL3 Study (Novo Nordisk)

Investigator: Prof. Dr. Martin Wabitsch  
Sponsor: Novo Nordisk A/S  
Duration: 2016 - 2020  
Partners: multiple partners (multinational study)  
Trial ID: NN8640-4172  

Growth hormone is crucial for physical development. Growth hormone is needed for normal growth in children. In adults, growth hormone is needed to maintain the proper amounts of body fat, muscle, and bone. Growth hormone deficiency (GHD) is caused by an inadequate secretion of growth hormone from the pituitary gland and leads to diverse physically and psychologically impairments. GHD negatively affects growth and body composition in childhood and adulthood.

Somapacitan or “NNC0195-0092” is a novel long-acting derivative of human growth hormone for treatment of children and adults with GHD. The children need to be pre-pubertal to avoid interference with the growth spurt during puberty with the treatment effect. The aim of the trial is to investigate efficacy and safety of Somapacitan treatment compared to the treatment with Norditropin® FlexPro® which is administered daily. Daily injections for years or lifetime can be inconvenient and distressing for patients. Somapacitan is designed to be administered only once weekly to improve convenience and compliance. The clinical trial is conducted multinational in different sites around the world, one of which is our Division of Paediatric Endocrinology and Diabetes at Ulm University Hospital.

Non-interventional, post-marketing surveillance “Saizen®-online”

Investigator: Prof. Dr. Martin Wabitsch  
Sponsor: Merck Serono  
Duration: since 2015 (15 years follow-up period)  
Partners: global partners (international phase IV study)  
Trial ID: EMR200104_544  

Saizen®, a recombinant human growth hormone (somatropin), is indicated for the treatment of growth hormone deficiency in children and adults, Turner Syndrome, chronic renal failure and children born short for gestational age (SGA). An observational, longitudinal, non-interventional, post-marketing surveillance programme has been initiated to assess the level of adherence under every day conditions and long-term safety and efficacy of therapy with Saizen® in a large number of patients. Our Division Division of Paediatric Endocrinology and Diabetes is one of the study centres involved in the global study.
Post-marketing surveillance to monitor the long-term safety and efficacy of Omnitrope® in infants, children and adolescents (PATRO Children)

Investigator: Prof. Dr. Martin Wabitsch
Sponsor: Sandoz Pharmaceuticals / Hexal AG
Duration: since 2016
Partners: global partners (international phase IV study)
Trial ID: EP00-501

Omnitrope®, a recombinant human growth hormone (somatropin) is used to treat children with growth disorders or genetic disorders like Turner syndrome and Prader-Willi syndrome. It is also used to treat adults with pronounced growth hormone deficiency. Omnitrope® has been used for over a decade since it has been marketed in Europe in 2006. However, some concerns remain about the long-term safety of Omnitrope®, which is administered to the patients on a daily basis. PATRO Children, an observational, longitudinal, non-interventional, post-marketing surveillance programme, investigates the long-term safety and effectiveness assessing the diabetogenic potential of Omnitrope and the risk of malignancies. Our Division of Paediatric Endocrinology and Diabetes is one of the study centres involved in the global study.

European Consortium of Lipodystrophies (ECLip) Registry

Speaker: Prof. Dr. Martin Wabitsch
Duration: since 2012
Partners: European Consortium of Lipodystrophies (ECLip)

Lipodystrophy syndromes are rare diseases characterised by selective deficiency of adipose tissue. They are categorised in different types based on aetiology (genetic or acquired) and distribution of lost adipose tissue affecting the entire body (generalised) or only regions (partial). Lipodystrophy is frequently associated high morbidity and mortality. Patients suffer from hormonal and metabolic disorders resulting in severe comorbidities. Lipodystrophy syndromes occur very rarely and the different types vary widely in their associated comorbidities, complications and courses. Even very experienced experts in this field do not see more than 50-100 patients in their lives. Due to the rarity of lipodystrophy syndromes and the lack of knowledge about these, physicians are unfamiliar with their diagnosis and management. Sensible clinical and basic research into rare diseases such as lipodystrophy syndromes is only possible in multi-location networks with sufficient case numbers. The European Consortium of Lipodystrophies (ECLip) is a network of European clinical and basic-science research groups working in the field of lipodystrophy syndromes. The network aims to increase the basic understanding of this rare disease and to develop ways to better diagnose, prevent and take in charge patients suffering from lipodystrophy syndromes. ECLip has launched a registry intended to improve the research conditions by consolidating information about lipodystrophy syndromes and collecting patient data on an international level. Upon informed consent, data obtained from patients during their clinical visits in participating centres (registry members) are being entered in a web-based registry platform. In our Centre for Rare Diseases (ZSE Ulm) at Ulm University Medical Center, we are treating patients with lipodystrophy syndromes. Our Division of Paediatric Endocrinology and Diabetes is the leading clinical centre coordinating the ECLip Registry. Ulm University is the governing body, the legal institution, where all data entered in the registry is stored. The ECLip Registry will enable the exchange of patient data for scientific evaluations and will help to recruit suitable subjects for clinical studies.
**Ulm Birth Cohort Study (UBCS) (‘Ulmer Kinderstudie’)**

**Investigators:** Prof. Dr. Hermann Brenner (German Cancer Research Center, Heidelberg), Prof. Dr. Dietrich Rothenbacher (Ulm University), Prof. Dr. Martin Wabitsch

**Funding:** Federal Ministry for Education and Research (BMBF), German Research Foundation (DFG)

**Duration:** since 2000

The Ulm Birth Cohort Study (UBCS) was initiated in 2001/2002 at the Department of Gynecology and Obstetrics of Ulm University Medical Center in order to investigate the impact of perinatal and neonatal factors on growth and metabolic diseases in adulthood (for example cardiovascular diseases, allergies, asthma and oncologic diseases). In total, over 1,000 mothers (including mothers with 22 pairs of twins) have agreed to participate in the study. At the time of the birth of the child, basic data have been collected using a questionnaire and biological samples have been obtained. Since then, the children and their parents have been followed up in regular, defined intervals for over 18 years.

One example of the meaningful results recently obtained from our studies: Circulating insulin concentrations reflect the metabolic cardiovascular risk and may trigger weight gain. The UBCS study showed that fasting plasma insulin concentrations of children are significantly correlated with the BMI values that mothers exhibit before pregnancy, and fasting plasma insulin concentrations of children are significantly correlated with maternal, but not with paternal fasting plasma insulin concentrations. Furthermore, the development of the BMI of a child with high fasting plasma insulin concentrations is altered compared to a child with low concentrations. These findings are in line with the concept of perinatal programming of insulin concentrations and BMI development by maternal factors.

**Diabetes and Social Jet Lag**

**Speaker:** Dr. Julia von Schnurbein

**Funding:** German Paediatric Diabetes Association (AGPD), Dr.-Herbert-Schiffers-Stiftung

**Duration:** 2013 - 2019

**Partners:** Dr. Claudia Boettcher (Justus Liebig University Giessen), Prof. Dr. Beate Karges (Bethlehem Gesundheitszentrum Stolberg gGmbH, RWTH Aachen University), Dr. Desiree Dunstheimer (Klinikum Augsburg), Dr. Angela Galler (Charité - Universitätsmedizin Berlin), Prof. Till Roenneberg (Ludwig-Maximilians-University Munich), Dr. Celine Vetter (Brigham and Women’s Hospital and Harvard Medical School Boston)

It is well known that lack of sleep increases the risk for development and deterioration of type 2 diabetes. The multicentre prospective study “Diabetes and Social Jet Lag” investigated the impact of lack of sleep, poor sleep quality and of a sleep timing unsuited to the patients natural sleep timing on blood sugar levels in patients with type 1 diabetes. The study showed that reduced sleep quality has a negative impact on HbA1c levels in patients with type 1 diabetes indicating that advice for a better sleep hygiene should maybe be integrated into the counseling of patients with diabetes.
Evidence-based harmonization of follow-up recommendations for endocrine late-effects of TOS and registries of the German Society for Pediatric Oncology and Hematology and development of a database module for the prospective evaluation of the follow-up guideline AWMF-no. 025-030

Speaker: PD Dr. Christian Denzer
Funding: Deutsche Kinderkrebsstiftung e.V. (DKS 2015.11)
Duration: 2015 - 2018
Partners: Prof. Dr. T. Langer, Universität zu Lübeck, Kinder- und Jugendmedizin

New treatment strategies have significantly improved the 5-year survival rate for childhood cancers in the past 40 years. Unfortunately, these treatments are associated with a markedly increased risk for late complications. Endocrine disorders are among the most common late effects, affecting 20 to 50% of survivors. In a preceding project funded by Deutsche Kinderkrebsstiftung (Project-Nr. DKS 2010/16), evidence-based guidelines for long-term endocrine follow-up have been developed by our group (S3 guideline “Endokrinologische Nachsorge nach onkologischen Erkrankungen im Kindes- und Jugendalter”, AWMF registry Nr. 025-030).

In our current project, we are revising follow-up recommendations for endocrine late-effects of all currently active as well as all closed therapy studies and registries for pediatric cancers of the GPOH e.V. using an exposure- and risk-centered approach. Harmonization of follow-up recommendations will have a major impact on the implementation of evidence-based clinical care and will furthermore provide the basis for standardized prospective documentation of endocrine late-effects using the well-established database structure of the ‘Late Effects Surveillance System’ (LESS, coordinator: Prof. T. Langer). Prospectively, this dataset will allow for systematic evaluation of current follow-up recommendations and will therefore contribute to continuous improvement of follow-up care.

Optimizing the RIST protocol for the treatment of Glioblastoma patients

Investigators: Dr. Mike-Andrew Westhoff, Dr. Lisa Nonnenmacher, Dr. Stephan Bartholomä, Prof. Dr. Klaus-Michael Debatin
Funding: Förderkreis für tumor- und leukämiekranke Kinder Ulm e.V.
Duration: ongoing

The multimodal RIST Protocol is a cyclic treatment approach where repeated treatment with two pharmacological inhibitors Rapamycin (Sirolimus) and Sprycel (Dasatinib) is followed by several doses of the two chemotherapeutic agents Inrinotecan and Temozolomide (TMZ) in a metronomic, low-dose setting. It was initially considered for the treatment of patients with recurrent or refractory Neuroblastoma (Corbacioglu et al., 2013), but has also been applied in a compassionate use setting for other paediatric tumours, such as Glioblastoma (Nonnenmacher et al., 2015). Importantly, the RIST treatment is associated with few side effects and, thus, a good quality of life is often associated with the treatment. Clinically, it significantly improves the life expectancy of approximately a third of the patients whose malignancy had been previously deemed untreatable.

Using our collection of over 100 patient-derived stem cell-like glioblastoma cells we are currently screening cell populations as to whether they respond to the RIST Protocol. Importantly, unlike those tumours presented in the context of the compassionate treatment, these
cells have not been previously exposed to chemo- and/or radiotherapy. Identifying good responders and non-responders we aim to ascertain which factors determine whether a tumour will be responsive to treatment and which additional pathways need to be targeted to convert non-responders to responders.

**Evaluation of preschool examination in Baden-Württemberg**

*Investigator:* Prof. Dr. Harald Bode  
*Sponsor:* Ministry of Social Affairs and Integration (State of Baden-Württemberg)  
*Partners:* 38 local health authorities, public health dept. of Baden-Württemberg  
*Duration:* 2015 - 2017

German federal states conduct preschool examinations of children to assess risks to their success in school. In 2009, step 1 of the preschool examination (ESU) in the German federal State Baden-Württemberg was preponed to the second-to-last year of kindergarten (age 4-5) to gain enough time for developmental interventions. Procedures and practice of ESU by local health authorities in step 1 and step 2 (last year of kindergarten) were analyzed from the data of about 90,000 ESUs and from local experiences to infer strengths, weaknesses and requirements for change in the ESU format. Recommendations for improving diagnostic methods and organization of ESU were given.

**Additional Projects in Brief**

- **GSC 270: International Graduate School in Molecular Medicine Ulm (IGradU)**  
  *Faculty from our lab:* Prof. Dr. Christian Beltinger, Prof. Dr. Klaus-Michael Debatin, Prof. Dr. Pamela Fischer-Posovszky, apl. Prof. Dr. Lüder H. Meyer, apl. Prof. Dr. Gudrun Strauß  
  *Coordinator:* Prof. Dr. Michael Kühl, Institute of Biochemistry and Molecular Biology  
  *Funding:* Excellence Initiative of the German Federal and State Governments  
  *Duration:* 2007 - 2019  
  *Partners:* Additional Departments and Institutes of Ulm University

- **Else Kröner Research College Ulm – Stem cells, aging and malignant transformation**  
  *Fellowship Dr. Julia Zinngrebe:* “Evaluation of mechanism of resistance against an IAP-antagonists-based therapy in acute lymphoblastic leukemia in children”;  
  *Fellowship Dr. Felix Seyfried:* “Identification und Charakterisierung genetischer Alterationen in apoptosedifizienten Hochrisiko Leukämien und Evaluierung neuer Therapiestrategien im NOD/SCID huALL Mausmodell”;  
  *(Supervisors: Prof. Dr. Klaus-Michael Debatin, apl. Prof. Dr. Lüder H. Meyer)*  
  *Fellowship Dr. Julia Würtemberger:* “PPP2CA as therapeutic target in neuroblastoma”  
  *(Supervisor: Prof. Dr. Christian Beltinger)*  
  *Coordinator:* Prof. Dr. Stephan Stilgenbauer, Department of Internal Medicine III  
  *Funding:* Else Kröner-Fresenius Stiftung  
  *Duration:* 2011 - 2018  
  *Partners:* Additional Departments and Institutes of Ulm University
MPN&MPNr Euronet (COST Action)

apl. Prof. Dr. Holger Cario

Coordinator: Dr. Sylvie Hermouet, University of Nantes
Duration: ongoing (externally funded 2009-2013)
Funding: COST Association
Partners: 128 Members in 28 Countries

European Congenital Erythrocytosis Consortium (ECE-C)

apl. Prof. Dr. Holger Cario

Curators: Celeste Bento (Portugal), Holger Cario (Ulm), Mary Frances McMullin (UK), François Girodon (France)
Duration: Ongoing since 2004
Partners: 15 Laboratories from Europe

International Osteopetrosis Registry

on behalf of the Inborn Error Working Party of the EBMT and the European Society of Immunodeficiencies

Coordinator: apl. Prof. Dr. Ansgar Schulz
Partners: multiple participating centres in Europe

Scientific Events

2018

Boehringer Ingelheim Ulm University BioCenter (BIU) – 6th Symposium

Organizer: Prof. Dr. Klaus-Michael Debatin, Dr. Lysann Palkowitsch
Partner: Medical Faculty, Boehringer Ingelheim
Date, Venue: 09.11.2018, Ulm

European Consortium of Lipodystrophies (ECLip) Registry Meeting

Organizers: Prof. Dr. Martin Wabitsch, Dr. Julia von Schnurbein
Partners: European Consortium of Lipodystrophies (ECLip)
Date, Venue: 22.10.2018, Ulm

Villa Vigoni Meeting – Cell Death and Disease

Organizer: Prof. Dr. Klaus-Michael Debatin
Partners: Profs. Krammer (Heidelberg/D), Simon (Bern/CH), Brancolini (Udine/I)
Date, Venue: 27.-30.06.2018, Loveno di Menaggio, Italy

6th Symposium of Hematology Today

Organizer: apl. Prof. Dr. Holger Cario
Partner: Dr. Stephan Lobitz (Köln)
Date, Venue: 19.-21.04.2018, Neu-Ulm
Scientific Events

- **BFM Plenary Meeting**
  - Organizer: Prof. Dr. Klaus-Michael Debatin, apl. Prof. Dr. Lüder H. Meyer
  - Partners: BFM Study Centers
  - Date, Venue: 22.-24.03.2018, Ulm

- **Training Event “The endocrinologic consultation”**
  - Organizer: Prof. Dr. Martin Wabitsch
  - Date, Venue: 23.-24.02.2018, Günzburg

2017

- **European Consortium of Lipodystrophies (ECLip) Registry Meeting**
  - Organizers: Prof. Dr. Martin Wabitsch, Dr. Julia von Schnurbein
  - Partner: European Consortium of Lipodystrophies (ECLip)
  - Date, Venue: 07.-08.07.2017, Ulm

- **Villa Vigoni Meeting – Cell Death and Disease**
  - Organizer: Prof. Dr. Klaus-Michael Debatin
  - Partners: Profs. Krammer (Heidelberg/D), Simon (Bern/CH), Brancolini (Udine/I)
  - Date, Venue: 14.-17.06.2017, Loveno di Menaggio, Italy

- **Boehringer Ingelheim Ulm University BioCenter (BIU) – 5th Symposium**
  - Organizer: Prof. Dr. Klaus-Michael Debatin, Dr. Lysann Palkowitsch
  - Partners: Medical Faculty, Boehringer Ingelheim
  - Date, Venue: 15.-16.05.2017, Ulm

- **Rare Disease Day**
  - Organizer: Prof. Dr. Klaus-Michael Debatin
  - Partner: Center for Rare Diseases (Zentrum für Seltene Erkrankungen – ZSE)
  - Date, Venue: 28.02.2017, Ulm

2016

- **1st Pediatric Cardiology Symposium**
  - Organizer: apl. Prof. Dr. Christian Apitz
  - Date, Venue: 03.12.2016, Ulm

- **52nd Workshop for Pediatric Research**
  - Organizer: Prof. Dr. Klaus-Michael Debatin
  - Partner: German Society of Pediatrics and Adolescent Medicine (DGKJ)
  - Date, Venue: 27.-28.10.2016, Frankfurt

- **Training Event “The endocrinologic consultation”**
  - Organizer: Prof. Dr. Martin Wabitsch
  - Date, Venue: 14.-15.10.2016, Günzburg
Advanced Seminar in Developmental Endocrinology, Developmental Biology of Gastrointestinal Hormones
Organizers: Prof. Dr. Martin Wabitsch, Dr. Anja Moss
Partner: European Society for Paediatric Endocrinology (ESPE)
Date, Venue: 03.-04.06.2016, Ulm

Half-yearly symposium of the South German Pediatric Endocrinologists
Organizers: PD Dr. Christian Denzer, Prof. Dr. Martin Wabitsch
Date, Venue: 16.04.2016, Ulm

Training Course in Social Pediatrics
Organizer: Prof. Dr. Harald Bode
Partner: Bezirksärztekammer Südwürttemberg
Date, Venue: 11.03., 12.03., 18.03., 19.03., 23.04.2016; Ulm

2015

Training Course in Social Pediatrics
Organizer: Prof. Dr. Harald Bode
Partner: Bezirksärztekammer Südwürttemberg

Training Event “The endocrinologic consultation”
Organizer: Prof. Dr. Martin Wabitsch
Date, Venue: 03.-04.07.2015, Günzburg

4th Symposium of Hematology Today: Hematology and Friends
Organizer: apl. Prof. Dr. Holger Cario
Partner: Dr. Stephan Lobitz (Berlin)
Date, Venue: 23.-25.04.2015, Ulm

51st Workshop for Pediatric Research
Organizer: Prof. Dr. Klaus-Michael Debatin
Partner: German Society of Pediatrics and Adolescent Medicine (DGKJ)
Date, Venue: 16.-17.04.2015, Göttingen

Boehringer Ingelheim Ulm University BioCenter (BIU) – 4th Symposium
Organizer: Prof. Dr. Klaus-Michael Debatin, Dr. Lysann Palkowitsch
Partners: Medical Faculty, Boehringer Ingelheim
Date, Venue: 14.04.2015, Ulm

8th Workshop in Neuropediatrics
Organizer: Prof. Dr. Harald Bode
Date, Venue: 18.03.2015, Ulm
Meetings of BMBF Network “Adolescents with Extreme Obesity”, YES-Study

Organizers: Prof. Dr. Martin Wabitsch, Dr. Julia von Schnurbein
Partner: Federal Ministry for Education and Research (BMBF)
Date, Venue: several meetings 2015-2018, Ulm
Prizes and Awards

2018

■ Dr. Salih Demir
Best oral contribution
11th Biennial Childhood Leukemia and Lymphoma Symposium, Helsinki, 2018

■ Dr. Kerstin Felgentreff
Margarete von Wrangell-Scholarship
(Habilitationsprogramm für Frauen)
State of Baden-Württemberg

■ Dr. Vera Münch
Franziska-Kolb Prize 2018
Franziska Kolb Foundation

■ Dr. Melanie Schirmer
STEPS-Award for “Deletionen auf Chromosom 16p11.2 sind assoziiert mit frühkindlicher Adipositas – 3 Fallberichte”
German Association for Pediatric Endocrinology and Diabetology (DGKED)

■ Dr. Hanna Schmidt
Hertha-Nathorff Scholarship
Medical Faculty, Ulm University

■ Felix Stirnweiß
Experimental Medicine Scholarship 2018
Medical Faculty, Ulm University

■ Dr. Mike-Andrew Westhoff
Teaching Award (Lehrbonus) 2018 for exceptional teaching qualities
Ulm University

■ Dr. Julia Zinngrebe
Margarete von Wrangell-Scholarship
(Habilitationsprogramm für Frauen)
State of Baden-Württemberg

■ Dr. Julia Zinngrebe
Invited Participation as Young Scientist
68th Lindau Nobel Laureate Meeting

2017

■ Dr. Stephanie Brandt
Hertha-Nathorff Scholarship
Medical Faculty, Ulm University

■ Elena Dorothea Brenner
Experimental Medicine Scholarship 2017/18
Medical Faculty, Ulm University

■ PD Dr. Christian Denzer
AGPD Abstract Award (AAA) for “Insulin-sensitivität und Betazellfunktion bei adipösen Kindern und Jugendlichen”, 2017
Arbeitsgemeinschaft für Pädiatrische Diabetologie (AGPD)

■ Prof. Dr. Pamela Fischer-Posovszky
Heisenberg Professorship, starting 2019
German Research Foundation (DFG)

■ Verena Janina Herbener
Experimental Medicine Scholarship 2017
Medical Faculty, Ulm University

■ Dr. Daniel Tews
STEPS-Award for “Stabile Überexpression von UCP1 in humanen Präadipozyten als ein Modell zur Untersuchung der braunen Fettzellfunktion”
German Association for Pediatric Endocrinology and Diabetology (DGKED)

■ Dr. Julia Zinngrebe
Doctoral Thesis Award
Ulmer Universitätsgesellschaft

■ Dr. Julia Zinngrebe
Hertha-Nathorff Scholarship
Medical Faculty, Ulm University

2016

■ Maximilian Auerhammer
Experimental Medicine Scholarship 2016/17
Medical Faculty, Ulm University
**Prizes and Awards**

- **Sophie Kiener**  
  Experimental Medicine Scholarship 2016/17  
  Medical Faculty, Ulm University

- **Malena Klingspor**  
  Experimental Medicine Scholarship 2016/17  
  Medical Faculty, Ulm University

- **Dr. Katja Kohlsdorf**  
  STEPS-Award for “Frühkindlicher BMI-Verlauf bei monogener Adipositas auf Basis einer Mutation im Leptin- oder Leptinrezeptor-Gen”  
  German Association for Pediatric Endocrinology and Diabetology (DGKED)

- **Dr. Johannes Krämer**  
  Research Funding 2016  
  German Association of Pediatric Cardiology (DGPK)

- **Malcom Meyer**  
  Experimental Medicine Scholarship 2016/17  
  Medical Faculty, Ulm University

- **Dr. Felix Seyfried**  
  2016 ASH Abstract Achievement Award  
  American Society of Hematology

- **Ning Wei**  
  Experimental Medicine Scholarship 2016  
  Medical Faculty, Ulm University

**2015**

- **Prof. Dr. Pamela Fischer-Posovszky**  
  Mileva-Einstein-Maric Prize 2015  
  Ulm University

- **Jan-Bernd Funcke**  
  Travel Grant DGKED/Merck Serono  
  German Association for Pediatric Endocrinology and Diabetology (DGKED)

- **Niklas Gäbler**  
  Experimental Medicine Scholarship 2015  
  Medical Faculty, Ulm University

- **Benedikt Haggenmüller**  
  Experimental Medicine Scholarship 2015  
  Medical Faculty, Ulm University

- **Sophia Neusser**  
  Experimental Medicine Scholarship 2014/15  
  Medical Faculty, Ulm University

- **PD Dr. Carsten Posovszky**  
  Ludwig-Demling Research Prize  
  German Crohn’s and Colitis Association (DCCV)

- **PD Dr. Carsten Posovszky**  
  Research Prize  
  German Speaking Society of Pediatric Gastroenterology and Nutrition (GPGE)

- **Julian Roos**  
  Science School “Non-coding RNAs in Paediatric Endocrinology” in Veyrier Le Lac, France  
  European Society for Paediatric Endocrinology

- **Julian Roos**  
  Travel grant “Forum Wachsen” 2015  
  German Association for Pediatric Endocrinology and Diabetology (DGKED)

- **Dr. Julia von Schnurbein**  
  Hertha-Nathorff Scholarship  
  Medical Faculty, Ulm University
Guest Scientists

2018

- **Belinda Lennerz, M.D., Ph.D.**
  Boston Children’s Hospital, Division of Endocrinology, USA
  regular visits in 2015-2018

2017

- **Ivana Vorgucin, M.D., Ph.D.**
  Institute for child and youth health care of Vojvodina, University of Novi Sad, Serbia
  ESPE Clinical Fellowship
  March-June 2017

- **Prof. Dr. Jiwu Wei**
  Jiangsu Key Laboratory of Molecular Medicine, Nanjing University, China

2016

- **Dr. Susanne Trombley**
  Uppsala University, Sweden
  June 2016

- **Dr. Agne Kulyte**
  Karolinska Institute, Stockholm, Sweden
  January 2016

2015

- **Dr. Maxime Denis**
  Montreal Heart Institute, Canada
  October 2015

- **Diya Trust**
  Staffordshire University, UK
  June-August 2015

- **Dr. Elena Inzaghi**
  University Tor Vergata, Rome, Italy
  January-February 2015

- **Fernando Tavares Fedumenti**
  Brazil
  October 2014-June 2015

International Cooperation Partners

- Children’s Cancer Institute Australia and Sydney Children’s Hospital, University of New South Wales, Sydney, Australia
- Center for Medical Genetics, Ghent University, Belgium
- Pediatric Stem Cell Transplantation, Willem Alexander Pediatric Hospital, Leiden University, Belgium
- Jiangsu Key Laboratory of Molecular Medicine, Nanjing University, China
- Minerva Foundation Institute for Medical Research, Helsinki, Finland
- Biocenter Oulu, University of Oulu, Finland
- Pediatric Immunology, Hematology and Rheumatology Unit, Necker-Enfants Malades Hospital, Paris, France
- Department of Bone Marrow Transplantation and Cancer Immunology, Hadassah Medical Center, Jerusalem, Israel
- Human Genome Lab, Humanitas Research Hospital, Milan, Italy
- Department of Women’s and Children’s Health, University of Padova, Italy
Doctorates Conferred

Dr. med. = MD; Dr. rer. nat. / Dr. biol. hum. = PhD

2018

- **Jan-Bernd Funcke, Dr. rer. nat.**
  Diagnosis and characterization of leptin mutation causing severe early-onset obesity

- **Annika Goß, Dr. rer. nat.**
  Oncolytic measles virus MV-NIS controls relapsed pediatric ALL patient-derived xenografts

- **Ines Mendler, Dr. med.**
  Anwendbarkeit und prädiktiver Wert des Thompson Scores bei Kindern mit perinataler Asphyxie im Rahmen der Hypothermietherapie

- **Eva Neuwirth, Dr. med.**
  Mortalität und Morbidität bei Ligatur des persistierenden Ductus Arteriosus Botalli bei Frühgeborenen unter 1500g auf einer neonatologischen Intensivstation

- **Lara Riehl, Dr. rer. nat**
  Targeted deep sequencing to identify novel blood biomarkers of neuroblastoma

- **Silke Streiftau, Dr. med.**
  Langfristige Entwicklungsprognose nach extremer Frühgeburttlichkeit

- **Franziska Stupp, Dr. med.**
  Lebensqualität und Elternzufriedenheit nach Adenotomie und Adenotonsillectomie im Kindesalter - Eine prospektive Studie -

- **Felix Zirngibl, Dr. med.**
  Attenuated oncolytic measles virus as a new therapeutic approach against pediatric acute lymphoblastic leukemia: a proof of principle (summa cum laude)

- **Verena Zoller, Dr. rer. nat.**
  Regulation of adipose tissue homeostasis by the death ligand TRAIL

2017

- **Ina Karen Alberts, Dr. med.**
  Leptin- und Adiponektingehalt im Nabelschnurblut und die Auswirkungen auf die Körperfettmasse sowie die Körperfettverteilung der Kinder

- **Louise Cypionka, Dr. med.**
  Übergewicht und Adipositas nach akuter lymphatischer Leukämie und Morbus Hodgkin im Kindes- und Jugendalter

- **Salih Demir, PhD**
  Restoration of mutant TP53 as a therapeutic targeting strategy in pediatric B-cell precursor acute lymphoblastic leukemia
Lioba Doornekamp-Zähr, Dr. med.
Prävalenz endokrinologischer Spätfolgen nach onkologischen Erkrankungen im Kindes- und Jugendalter - eine unizentrische Fallserienuntersuchung

Stefanie Havers, Dr. med.
Zerebrale Oxygenierung während der postnatalen Adaption von Neugeborenen in Abhängigkeit des Geburtsmodus und Gestationsalters

Clarissa Klein, Dr. med.
Verifikation potentieller Interaktionspartner des Zellzyklusregulators p27Kip1

Kathy Kohleis, Dr. biol. hum.
Seelische Gesundheit von Kindern und Jugendlichen mit infantiler Zerebralparese und Spina bifida

Joanna Meßmann, Dr. rer. nat.
Myeloid-derived suppressor cells (MDSCs) as modulators of graft-versus-host disease (GVHD)

Vera Münch, Dr. rer. nat.
VEGF – A Novel Therapeutic Target in Central Nervous System Acute Lymphoblastic Leukaemia

Nicola Roßmann, Dr. med.
Verlauf und Outcome der Anwendung von permissiver Hyperkapnie bei immun-supprimierten Kindern mit Atemversagen

Kolja Sievert, Dr. med.
Inpatient Long-Term Therapy for Extremley Obese Adolescents and Young Adults: Reduction of the Visceral Fat and Improvement of Cardiovascular Risk Profile

Sebastian Ulrich, Dr. med.
The Death-Associated Protein Kinase 1 (DAPK1) - prognostic relevance in pediatric acute lymphoblastic leukemia (ALL) and evaluation as a therapeutic target

Julia Zinngrebe, Dr. med.
The role of linear ubiquitination in toll-like receptor 3 signalling (summa cum laude)

2016

Richard Blossey, Dr. med.
Die Bedeutung der Zelltodinduktion bei der in vitro Interaktion von MDSCs und T-Zellen

Amina Hochweber, Dr. med.
Die Entwicklung von Körpergewicht und Körpergröße von Geburt bis zum Schulalter bei Ulmer Schulkindern

Daniela Holzner, Dr. med.
Thyreoidale Dysfunktion und Steatosis hepatis bei übergewichtigen Kindern und Jugendlichen

Hannah Kunze, Dr. med.
Die Bedeutung phosphorylierter Signaltransduktionsproteine in der akuten pädiatrischen lymphoblastischen Leukämie

Verena Panitz, Dr. med.
Regulation of human granzyme B-producing plasmacytoid dendritic cells by viral stimuli

Matthias Schneider, Dr. med.
A paired comparison between glioblastoma cancer stem cells and differentiated cells in view of proliferation, resistance to conventional therapies and tumour-initiating capabilities

Felix Seyfried, Dr. med.
Characterization of aspects of leukemia biology and association with patient prognosis (summa cum laude)
Jana Stursberg, Dr. med.
Charakterisierung prognostischer Faktoren der pädiatrischen akuten lymphatischen Leukämie auf Genexpressions- und funktioneller Ebene

Ivana Zagotta, PhD
The Effect of Resveratrol on Obesity Associated Fibrosis in Adipocytes

2015

Eveliina Enlund, PhD
Role of MicroRNAs in the Pathophysiology of Obesity

Md. Nabiul Hasan, Dr. biol. hum.
Targeting of hyperactivated mTOR signaling in high-risk acute lymphoblastic leukemia as a novel treatment strategy

Habilitations Conferred

2018

Christian Denzer, PD Dr. med.
Körperliche Entwicklung und metabolische Komorbidität bei adipösen Kindern und Jugendlichen

2015

Carsten Posovszky, PD Dr. med.
Pathophysiologie angeborener Erkrankungen des Intestinums

Catharina Schütz, PD Dr. med.
Monogenic immunodeficiencies: a spectrum from severe immunodeficiency to mild immune dysregulation with emphasis on RAG deficiencies
1. **Point shear wave elastography of the pancreas in patients with cystic fibrosis: a comparison with healthy controls.**

   **Abdom Radiol (NY).** 2018; 43(9): 2384-2390 (IF=1.506)

2. **BARI-AD: Leitlinien-basiertes Interview als Grundlage psychologischer Stellungnahmen vor einem Adipositas-chirurgischen Eingriff bei Adoleszenten**

   **Adipositas.** 2018; 12(03): 134-142

3. **Epidemiology of the Übergewicht and der Adipositas bei Kindern in Kinder- und Jugendlichen anhand deutscher Schuleingangsdaten**

   **Adipositas.** 2018; 12(01): 10-15

4. **True Colours - Heterogenität des Fettgewebes**

   **Adipositas.** 2018; 12(04): 193-197

5. **Monogene Formen der Adipositas beim Menschen**

   **Adipositas.** 2018; 12(04): 162-167

6. **Kongressausgabe zur 34. Jahrestagung der DAG und zur 12. Diabetes Herbsttagung der DDG**

   **Adipositas.** 2018; 12(03): 109-109

7. **Distinct Effects of IL-6 Classic and Trans-Signaling in Bone Fracture Healing.**

   **Am J Pathol.** 2018; 188(2): 474-490 (IF=4.069)

8. **Efficacy and safety of methylene blue in the treatment of malaria: a systematic review.**

   **BMC Med.** 2018; 16(1): 59 (IF=9.088)

9. **IL7R is associated with CNS infiltration and relapse in pediatric B-cell precursor acute lymphoblastic leukemia.**

   **Blood.** 2018; 132(15): 1614-1617 (IF=15.132)

10. **Identification of a new exon and complex splicing alterations in familial erythrocytosis or von Hippel-Lindau disease.**

    **Blood.** 2018; 132(5): 469-483 (IF=15.132)

11. **Tight regulation of FOXO1 is essential for maintenance of B-cell precursor acute lymphoblastic leukemia.**

    **Blood.** 2018; 131(26): 2929-2942 (IF=15.132)

12. **Daratumumab in life-threatening autoimmune hemolytic anemia following hematopoietic stem cell transplantation.**

    **Blood Adv.** 2018; 2(19): 2550-2553

13. **Effective treatment of steroid and therapy-refractory acute graft-versus-host disease with a novel mesenchymal stromal cell product (MSC-FFM).**

    **Bone Marrow Transplant.** 2018; 53(7): 852-862 (IF=4.497)

14. **Diagnosis and severity criteria for sinusoidal obstruction syndrome/veno-occlusive disease in pediatric patients: a new classification from the European society for blood and marrow transplantation.**

    **Bone Marrow Transplant.** 2018; 53(2): 138-145 (IF=4.497)

15. **Recent advances in understanding the pathogenesis and management of reticular dysgenesis.**

    **Br J Haematol.** 2018; 180(5): 644-653 (IF=5.128)

16. **Hoenig M, Pannicke U, Gaspar HB, Schwarz K**
16. Low incidence of symptomatic osteonecrosis after allogeneic HSCT in children with high-risk or relapsed ALL - results of the ALL-SCT 2003 trial.


Cell Death Differ. 2018; 25(3): 486-541 (IF=8.000)


Cell Death Dis. 2018; 9(2): 116 (IF=5.638)

Westhoff MA, Marschall NJ, Grunert M, Karpel-Massler G, Burdach S, Debatin KM


Clin Cancer Res. 2018; 24(22): 5772-5783 (IF=10.199)


20. Metabolic Reprogramming by Dual AKT/ERK Inhibition through Imipridones Elicits Unique Vulnerabilities in Glioblastoma.

Clin Cancer Res. 2018; 24(21): 5392-5406 (IF=10.199)


21. Combined HDAC and Bromodomain Protein Inhibition Reprograms Tumor Cell Metabolism and Elicits Synthetic Lethality in Glioblastoma.

Clin Cancer Res. 2018; 24(16): 3941-3954 (IF=10.199)


22. Targeted inhibition of CD74 attenuates adipose COX-2-MIF-mediated M1 macrophage polarization and retards obesity-related adipose tissue inflammation and insulin resistance.


Chan PC, Wu TN, Chen YC, Lu CH, Wabitsch M, Tian YF, Hsieh PS

23. Radiation and Brain Tumors: An Overview.


24. Area Deprivation and Regional Disparities in Treatment and Outcome Quality of 29,284 Pediatric Patients With Type 1 Diabetes in Germany: A Cross-sectional Multicenter DPV Analysis.

Diabetes Care. 2018; 41(12): 2517-2525 (IF=13.397)


25. Increased thiF202b/thiF16 expression stimulates adipogenesis in mice and humans.

Diabetologia. 2018; 61(5): 1167-1179 (IF=6.023)

41. **MYOSB, STX3, and STXBP2 mutations reveal a common disease mechanism that unifies a subset of congenital diarrheal disorders: A mutation update.** *Hum Mutat.* 2018; 39(3): 333-344 (IF=5.359)
Dheke HS, Pylpynenko O, Overeem AW, Ferreira RJ, van der Velde KJ, Rings EHHM, Posovsky C, Swertz MA, Houdusse A, van Uzendonk SCD

42. **Targeted therapy of pulmonary arterial hypertension: Updated recommendations from the Cologne Consensus Conference 2018.** *Int J Cardiol.* 2018; 272S: 37-45 (IF=4.034)

43. **Pulmonary hypertension in adults with congenital heart disease: Updated recommendations from the Cologne Consensus Conference 2018.** *Int J Cardiol.* 2018; 272S: 79-88 (IF=4.034)


45. **Impact of X-ray Exposure on the Proliferation and Differentiation of Human Pre-Adipocytes.** *Int J Mol Sci.* 2018; 19(9) (IF=3.687)

46. **Early childhood BMI trajectories in monogenic obesity due to leptin, leptin receptor, and melanocortin 4 receptor deficiency.** *Int J Obes (Lond).* 2018; 42(9): 1602-1609 (IF=5.151)

47. **Inhibition of PI3K signalling increases the efficiency of radiotherapy in glioblastoma cells.** *Int J Oncol.* 2018; 53(5): 1881-1896 (IF=3.33)


56. Trajectories of Body Mass Index from Childhood to Young Adulthood among Patients with Type 1 Diabetes—A Longitudinal Group-Based Modeling Approach Based on the DPV Registry. J Pediatr. 2018; 201: 78-85.e4 (IF=3.667)


von Scheidt F, Eicken A, Wowra T, Brunner H, Apitz C


Cario H


Burdach SEG, Westhoff MA, Steinhauser MF, Debatin KM


Schleker T, Jacobsen EM, Mayer B, Strauss G, Debatin KM, Posovsky C


63. Extracellular Vesicles from Hypoxic Adipocytes and Obese Subjects Reduce Insulin-Stimulated Glucose Uptake. Mol Nutr Food Res. 2018; 62(S) (IF=5.151)

Mleczko J, Ortega FJ, Falcon-Perez JM, Wabitsch M, Fernandez-Real JM, Mora S

64. Hemoglobinopathies as a challenge of migrant medicine. Monatsschr Kinderheilkd. 2018; 166(11): 968-976 (IF=0.23)

Cario H, Lobitz S

65. Strategies to combat the obesity epidemic. Monatsschr Kinderheilkd. 2018; 166(5): 386-387 (IF=0.23)

Koletzko B, Wabitsch M
66. Vitamin D supplementation beyond the second year of life. Joint statement of the Nutrition Committee of the German Society for Pediatric and Adolescent Medicine (DGJK) and the German Society for Pediatric Endocrinology and Diabetology (DGKED) 
*Monatsschr Kinderheilk.* 2018; 166(9): 814-822 (IF=0.23)


67. Monogenic obesity. New diagnostic and therapeutic options 
*Monatsschr Kinderheilk.* 2018; 166(5): 388-394 (IF=0.23)

von Schnurbein J, Borck G, Hinney A, Wabitsch M

68. NOX1 loss-of-function genetic variants in patients with inflammatory bowel disease. 
*Mucosal Immunol.* 2018; 11(2): 562-574 (IF=7.36)


69. Pharmacological inhibition of IL-6 trans-signaling improves compromised fracture healing after severe trauma. 
*Naunyn Schmiedebergs Arch Pharmacol.* 2018; 391(5): 523-536 (IF=2.238)


70. Predictive Value of Thompson-Score for Long-Term Neurological and Cognitive Outcome in Term Newborns with Perinatal Asphyxia and Hypoxic-Ischemic Encephalopathy Undergoing Undercontrolled Hypothermia Treatment. 
*Neonatology.* 2018; 114(4): 341-347 (IF=2.688)

Mendler MR, Mendler I, Hassan MA, Mayer B, Bode H, Hummler HD

71. Influence of PCO2 Control on Clinical and Neurodevelopmental Outcomes of Extremely Low Birth Weight Infants. 
*Neonatology.* 2018; 113(3): 221-230 (IF=2.688)


72. Human Milk Oligosaccharides: 2'-Fucosyllactose (2'-FL) and Lacto-N-Neotetraose (LNNT) in Infant Formula. 
*Nutrients.* 2018; 10(9) (IF=4.196)


73. Current Guidelines for Obesity Prevention in Childhood and Adolescence. 
*Obes Facts.* 2018; 11(3): 263-276 (IF=3.108)


74. Viability of glioblastoma stem cells is effectively reduced by disiothiocyanate-derived mercapturic acids. 
*Oncol Lett.* 2018; 16(5): 6181-6187 (IF=1.664)


75. Proof-of-principle that a decoy virus protects oncolytic measles virus against neutralizing antibodies. 
*Oncolytic Virotion.* 2018; 7: 37-41

Xu C, Goß AV, Dorneburg C, Debatin KM, Wei J, Betzinger C

76. The therapeutic properties of resinostat for hepatocellular carcinoma. 
*Oncoscience.* 2018; 5(5-6): 196-208

Zhao J, Gray SG, Wabitsch M, Greene CM, Lawless MW

77. [Morphological characteristics of osteopetrosis]. 
*Patholohoe.* 2018; 39(2): 164-171 (IF=0.555)


78. CNS progression during vinblastine or targeted therapies for high-risk relapsed ALK-positive anaplastic large cell lymphoma: A case series. 
*Pediatr Blood Cancer.* 2018; 65(6): e27003 (IF=2.646)

Ruf S, Hebart H, Hajlgrim LL, Kabickova E, Lang P, Steinbach D, Schwabe GC, Woessmann W

*Pediatr Cardiol.* 2018; 39(6): 1115-1122 (IF=1.54)


80. Long-term study of tubeless insulin pump therapy compared to multiple daily injections in youth with type 1 diabetes: Data from the German/Austrian DPV registry. 

Danne T, Schwandt A, Biester T, Heidtmann B, Rami-Merhar B, Haberland H, Müller S, KhodaVerdi S, Haak T, Hol RW, DPV Initiative
81. Continuous glucose monitoring and glycemic control among youth with type 1 diabetes: International comparison from the T1D Exchange and DPV Initiative. 

DeSalvo DJ, Miller KM, Herrmann JM, Maahs DM, Hofer SE, Clements MA, Lilienthal E, Sherr JL, Tauschmann M, Holl RW, T1D Exchange and DPV Registries

82. Metabolic control of type 1 diabetes in youth with autism spectrum disorder: A multicenter Diabetes-Patienten-Verlaufsdocumentation analysis based on 61,749 patients up to 20 years of age. 


83. Risk of recurrent severe hypoglycemia remains associated with a past history of severe hypoglycemia up to 4 years: Results from a large prospective contemporary pediatric cohort of the DPV initiative. 


84. Sleep and glycemic control in adolescents with type 1 diabetes. 


85. Presentation of pediatric Henoch-Schönlein purpura nephritis changes with age and renal histology depends on biopsy timing. 

Pediatr Nephrol. 2018; 33(12): 277-286 (IF=2.627) 

86. Outcome of membranoproliferative glomerulonephritis and C3-glomerulopathy in children and adolescents. 

Pediatr Nephrol. 2018; 33(12): 2289-2298 (IF=2.627) 
Holle J, Berenberg-Goßler L, Wu K, Beringer O, Kropf P, Müller D, Thumfart J

87. Circulating levels of miR-122 and nonalcoholic fatty liver disease in pre-pubertal obese children. 

Pediatr Obes. 2018; 13(3): 175-182 (IF=3.98) 

88. Creation of a restrictive atrial communication in pulmonary arterial hypertension (PAH): effective palliation of syncope and end-stage heart failure. 

Pulm Circ. 2018; 8(2): 2045894018776518 (IF=2.283) 
Bauer A, Khalil M, Schmidt D, Bauer J, Esmaeili A, Apitz C, Voelkel NF, Schranz D

89. Sildenafil-Bosentan Drug-Drug Interaction: A Word of Caution Regarding the Most Common Combination Therapy in Children with Advanced Pulmonary Arterial Hypertension. 

Respiration. 2018; 96(3): 302 (IF=2.591) 
Apitz C, Schranz D

90. MiR-744-5p inducing cell death by directly targeting HNRNPC and NFIX in ovarian cancer cells. 


92. DEHP deregulates adipokine levels and impairs fatty acid storage in human SGBS-adipocytes. 


93. Dual Inhibition of Bcl-2/Bcl-xL and XPO1 is synthetically lethal in glioblastoma model systems. 

Shang E, Zhang Y, Shu C, Ishida CT, Bianchetti E, Westhoff MA, Karpel-Massler G, Siegelin MD

94. Inhibition of Bcl-2/Bcl-xL and c-MET causes synthetic lethality in model systems of glioblastoma. 

Zhang Y, Ishida CT, Shu C, Kleiner G, Sanchez-Quintero MJ, Bianchetti E, Quinzii CM, Westhoff MA, Karpel-Massler G, Siegelin MD

95. Effects of Levetiracetam and Lamotrigine on EEG in benign epilepsy with centrotemporal spikes: A randomized controlled trial. 

Seizure. 2018; 56: 115-120 (IF=2.839) 


Transfusion. 2018; 58(11): 2495-2500 (IF=3.423) 
Publications in Scientific Journals


2017


111. Predictors of health-related quality of life in children with chronic heart disease. *Cardiol Young.* 2017; 27(8): 1455-1464 ([IF=0.978](https://doi.org/10.1017/S1047951116005187))


Hammer E, Lilienthal E, Hefer SO, Schulz S, Bollow B, Höll RW, DPV Initiative and the German BMWF Competence Network for Diabetes Mellitus


Craig ME, Prinz N, Boyle CT, Campbell FM, Jones TW, Hofer SE, Simmons JH, Holman N, Tham E, Fröhlich-Reiterer E, DuBose S, Thornton H, King B, Maahs DM, Holl RW, Warner JT, Australasian Diabetes Data Network (ADDN), the T1D Exchange Clinic Network (T1DX), the National Paediatric Diabetes Audit (NPDA) and the Royal College of Paediatrics and Child Health, Prospective Diabetes Follow-up Registry (DPV) initiative


Craig ME, Prinz N, Boyle CT, Campbell FM, Jones TW, Hofer SE, Simmons JH, Holman N, Tham E, Fröhlich-Reiterer E, DuBose S, Thornton H, King B, Maahs DM, Holl RW, Warner JT, Australasian Diabetes Data Network (ADDN), the T1D Exchange Clinic Network (T1DX), the National Paediatric Diabetes Audit (NPDA) and the Royal College of Paediatrics and Child Health, Prospective Diabetes Follow-up Registry (DPV) initiative

118. Longitudinal Trajectories of Metabolic Control From Childhood to Young Adulthood in Type 1 Diabetes From a Large German/Austrian Registry: A Group-Based Modeling Approach. *Diabetes Care.* 2017; 40(3): 309-316 ([IF=13.397](https://doi.org/10.2337/dc16-2101))


Posovszky C


Wabitsch M


Wabitsch M


Karpel-Massler G, Ishida CT, Zhang Y, Halatsch ME, Westhoff MA, Siegelin MD

127. Cerebral Microstructural Alterations after Radiation Therapy in High-Grade Glioma: A Diffusion Tensor Imaging-Based Study. **Front Neurol.** 2017; 8: 286 (IF=3.508)
Kassubeck R, Gorges M, Westhoff MA, Ludolph AC, Kassubeck J, Müller HP

128. Recent Progress of the AREgPKD Registry Study on Autosomal Recessive Polycystic Kidney Disease. **Front Pediatr.** 2017; 5: 18 (IF=2.335)
Ebner K, Schaefer F, Liebau MC, AREgPKD Consortium (including Beringer O)

129. Inflammatory Mediators in Tracheal Aspirates of Preterm Infants Participating in a Randomized Trial of Permissive Hypercapnia. **Front Pediatr.** 2017; 5: 246 (IF=2.335)


133. Building a National Framework for Adolescent and Young Adult Hematology and Oncology and Transition from Pediatric to Adult Care: Report of the inaugural Meeting of the “AJET” Working Group of the German Society for Pediatric Oncology and Hematology. **J Adolesc Young Adult Oncol.** 2017; 6(2): 194-199 (IF=2.167)

134. Severe glucose-6-phosphate dehydrogenase deficiency leads to susceptibility to infection and absent NETosis. **J Allergy Clin Immunol.** 2017; 139(1): 212-219.e3 (IF=13.258)


136. Mast Cells Are Critical Regulators of Bone Fracture-Induced Inflammation and Osteoclast Formation and Activity. **J Bone Miner Res.** 2017; 32(12): 2431-2444 (IF=6.314)


138. Vedolizumab in Paediatric Inflammatory Bowel Disease: A Retrospective Multi-Centre Experience From the Paediatric IBD Porto Group of ESPGHAN. **J Crohns Colitis.** 2017; 11(10): 1230-1237 (IF=6.637)

Schoch J, Rohrer TR, Kaestner M, Abdul-Khaliq H, Gortner L, Sester U, Sester M, Schmidt T

142. Pulmonale und pulmonalarterielle Hypertonie bei Erwachsenen mit angeborenen Herzfehlern

*Journal für angeborene Herzfehler.* 2017; 112(1): 40-46 (IF=2.688)

143. „Migrantenanämien“ oder „Migrationsanämie“. Neue Worte für alte Erkrankungen

*Kinder- und Jugendmedizin.* 2017; 17(2): 75-80

144. Osteonecrosis develops independently from radiological leukemic infiltration of bone in adolescents with acute lymphoblastic leukemia - first findings of the OPAL trial.

*Leuk Lymphoma.* 2017; 29(4): 360-364 (IF=0.213)

145. The histone deacetylase inhibitor givinostat (ITF2357) exhibits potent anti-tumor activity against CRLF2-rearranged BCP-ALL.

*Leukemia.* 2017; 31(11): 2365-2375 (IF=10.023)

146. Frühkindlicher BMI-Verlauf bei monogener Adipositas

*Med Genet.* 2017; 29(4): 360-364 (IF=0.213)

147. Lipodystrophie-Erkrankungen

*Med Genet.* 2017; 29(4): 374-388 (IF=0.213)

148. Zu viel Fett – zu wenig Fett

*Med Genet.* 2017; 29(4): 347-347 (IF=0.213)

149. Monogene Adipositas

*Med Genet.* 2017; 29(4): 348-359 (IF=0.213)

150. Teneurin-2 (TENM2) deficiency induces UCP1 expression in differentiating human fat cells.

*Mol Cell Endocrinol.* 2017; 443: 106-113 (IF=3.563)

151. Estimated prevalence of potentially damaging variants in the leptin gene.


152. Differential expression of serpins may selectively licence distinct granzyme B functions including antigen cross-presentation.

*Mol Immunol.* 2017; 87: 325-326 (IF=3.188)


*Mol Metab.* 2017; 6(10): 1226-1239 (IF=6.291)

154. Treatment of pulmonary hypertension associated with congenital heart disease

*Monatsschr Kinderheilkd.* 2017; 165(11): 972-981 (IF=0.230)

155. Physiological relevance of brown adipose tissue in humans

*Monatsschr Kinderheilkd.* 2017; 165(6): 502-509 (IF=0.230)

156. Transcription factor Hlx controls a systematic switch from white to brown fat through Prdm16-mediated co-activation.


*Neonatology.* 2017; 112(1): 40-46 (IF=2.688)

158. Tidal Volume Delivery and Endotracheal Tube Leak during Cardiopulmonary Resuscitation in Intubated Newborn Piglets with Hypoxic Cardiac Arrest Exposed to Different Modes of Ventilatory Support.

*Neonatology.* 2017; 111(2): 100-106 (IF=2.688)

159. Anti-glioma Activity of Dapsone and Its Enhancement by Synthetic Chemical Modification.

*Neurochem Res.* 2017; 42(12): 3382-3389 (IF=2.772)

160. Disrupted apical exocytosis of cargo vesicles causes enteropathy in FHL5 patients with Munc18-2 mutations.

*JCI Insight.* 2017; 2(14): e94564

161. Disrupted apical exocytosis of cargo vesicles causes enteropathy in FHL5 patients with Munc18-2 mutations.

*JCI Insight.* 2017; 2(14): e94564
160. Simultaneous Interference with HER1/EGFR and RAC1 Signaling Drives Cytostasis and Suppression of Survivin in Human Glioma Cells In Vitro. Neurochem Res. 2017; 42(5): 1543-1554 (IF=2.772)


165. BH3-mimetics and BET-inhibitors elicit enhanced lethality in malignant glioma. Oncotarget. 2017; 8(18): 29558-29573
Ishida CT, Bianchetti E, Shu C, Halatsch ME, Westhoff MA, Karpel-Massler G, Siegelin MD

166. Mitochondrial matrix chaperone and c-myc inhibition causes enhanced lethality in glioblastoma. Oncotarget. 2017; 8(23): 37140-37153
Ishida CT, Shu C, Halatsch ME, Westhoff MA, Altieri DC, Karpel-Massler G, Siegelin MD


Laube M, Amann E, Uhlig U, Yang Y, Fuchs HW, Zemlin M, Mercier JC, Maier RF, Hummler HD, Uhlig S, Thome UH

171. Diagnostics in Children and Adolescents with Suspected or Confirmed Pulmonary Hypertension. Paediatr Respir Rev. 2017; 23: 3-15 (IF=2.354)
Koestenberger M, Hansmann G, Apitz C, Latus H, Lammers A

172. The epidemiology of sickle cell disease in Germany following recent large-scale immigration. Pediatr Blood Cancer. 2017; 64(7) (IF=2.646)

Latus H, Wagner J, Ostermayer S, Kerst G, Kreuder J, Schranz D, Apitz C


Dost A, Bechtold-Dalla Pozza S, Bollow E, Vogel P, Feldhahn L, Schwab KO, Holl RW, Initiative DPV


177. PLA2R-positive (primary) membranous nephropathy in a child with IPEX syndrome. Pediatr Nephrol. 2017; 32(9): 1621-1624 (IF=2.627)
Chuva T, Pfister F, Beringer O, Felgentreff K, Büttner-Herold M, Amann K

Kaltenbach TE, Graeter T, Oeztuerk S, Holzer D, Kratzer W, Wabitsch M, Denzer C

180. Splenic glucocorticoid resistance following psychosocial stress requires physical injury. 
Foertsch S, Füchsl AM, Faller SD, Hölszer H, Langgartner D, Messmann J, Strauß G, Reber SO

181. MDSCs are induced after experimental blunt chest trauma and subsequently alter antigen-specific T cell responses. 

182. Cardiac Depression in Pigs after Multiple Trauma - Characterization of Posttraumatic Structural and Functional Alterations. 

183. Subcutaneous white adipocytes express a light sensitive signaling pathway mediated via a melanopsin/TRPC channel axis. 


185. Sport mit angeborenem Herzfehler - Wo stehen wir 2017? 
Swiss Sports & Exercise Medicine. 2017; 65(3): 60-64
Siaplaouras J, Albrecht C, Apitz C

186. A case of anti-Rd causing fetal anemia. 
Transfusion. 2017; 57(6): 1485-1487 (IF=3.423)
Rauch S, Rütgen J, Wüskirchen M, Bauerfeind U, Kohne E, Weinstock C

Frömmel C, Kohne E

188. TLRs Go Linear - On the Ubiquitin Edge. 
Emmgrebe J, Walczak H

189. Cancer stem cells: The potential role of autophagy, proteolysis, and cathepsins in glioblastoma stem cells. 
Tumor Biol. 2017; 39(3): 1010428317692227

190. [EXIT - A Possible Intervention for New- and Earlyborn Babies with Severe Hydrops Fetalis and Hydrothoraces on Both Sides]. 
Z Geburtschile Neonatol. 2017; 221(6): 286-290 (IF=0.246)
Koch S, Essers J, Beringer O, Reister F, Hummler H, Moewes A

191. Mild Hypothermia in a Child with Low-Dose Risperidone. 
Z Kinder Jugendpsychiatr Psychother. 2017; 45(4): 335-337 (IF=1.206)
Grau K, Plener PL, Gahr M, Denzer C, Freudenmann RW

2016

192. Novel Approaches to Apoptosis-Inducing Therapies. 
Westhoff MA, Marschall N, Debatin KM

193. LNK mutations and myeloproliferative disorders. 
McMullin MF, Carlo H

194. Prehepatic secretion and disposal of insulin in obese adolescents as estimated by three-hour, eight-sample oral glucose tolerance tests. 
Am J Physiol Endocrinol Metab. 2016; 311(1): E82-94 (IF=4.142)
Vogt JA, Domzic J, Wabitsch M, Denzer C

195. Insulin/glucose induces natriuretic peptide clearance receptor in human adipocytes: a metabolic link with the cardiac natriuretic pathway. 

196. Development and psychometric validation of the ‘Parent Perspective University of Rhode Island Change Assessment-Short’ (PURICA-S) Questionnaire for the application in parents of children with overweight and obesity. 
BMJ Open. 2016; 6(11): e012711 (IF=2.369)

Posovszky C

198. Resveratrol inhibits lipogenesis of 3T3-L1 and SGBS cells by inhibition of insulin signaling and mitochondrial mass increase. 
199. MicroRNA-192* impairs adipocyte triglyceride storage.
*Biochim Biophys Acta.* 2016; 1861(4): 342-351
(IF=4.702)

(IF=4.704)

201. Impact of genotype on endocrinological complications in β-thalassemia patients.

202. Mutations in AP3D1 associated with immunodeficiency and seizures define a new type of Hermansky-Pudlak syndrome.
*Blood.* 2016; 127(8): 997-1006
(AIF=13.164)

203. The minimum required level of donor chimerism in hereditary hemophagocytic lymphohistiocytosis.
*Blood.* 2016; 127(25): 3281-90
(IF=13.164)

*Blood.* 2016; 128(3): 440-8
(IF=13.164)

205. Regulation and Function of Lentiviral Vector-Mediated TCRiG1 Expression in Osteoclasts from Patients with Infantile Malignant Osteopetrosis: Implications for Gene Therapy.
*Calcif Tissue Int.* 2016; 99(6): 638-648
(IF=3.124)
Thudium CS, Moscatelli I, Loßhail H, Kertész Z, Montano C, Bjurstöm CF, Karsdal MA, Schulz A, Richter J, Henriksen K

206. Cathepsin G-mediated proteolytic degradation of MHC class I molecules to facilitate immune detection of human glioblastoma cells.
*Cancer Immunol Immunother.* 2016; 65(3): 283-91
(IF=4.711)

207. Boolean modeling identifies Grewalt/MASTL as an important regulator in the AURKA network of neuroblastoma.
*Cancer Lett.* 2016; 371(1): 79-89
(IF=6.375)

*Cell Death Dis.* 2016; 7: e2052
(IF=5.965)
Schirmer M, Trentin L, Queudeville M, Seyfried F, Demir S, Tausch E, Stitigenbauer S, Eckhoff SM, Meyer LH, Debatin KM

209. TRAIL (TNF-related apoptosis-inducing ligand) inhibits human adipocyte differentiation via caspase-mediated downregulation of adipogenic transcription factors.
*Cell Death Dis.* 2016; 7(10): e2142
(IF=5.965)

*Crit Rev Oncog.* 2016; 21(3-4): 253-267

211. Zerebraler Krampfanfall – Ein Leitfaden zur prähospitalen Diagnosefindung und Therapie
*Der Notarzt.* 2016; 32(01): 40-45
Harth A, Winter B, Kulla M

212. International Comparison of Smoking and Metabolic Control in Patients With Type 1 Diabetes.
*Diabetes Care.* 2016; 39(10): e177-8
(IF=11.857)

213. Does β-Cell Autoimmunity Play a Role in Cystic Fibrosis-Related Diabetes? Analysis Based on the German/Austrian Diabetes Patienten Verlaufs dokumentation Registry.
*Diabetes Care.* 2016; 39(8): 1338-44
(IF=11.857)

214. Trend of antihyperglycaemic therapy and glycaemic control in 184,864 adults with type 1 or 2 diabetes between 2002 and 2014: Analysis of real-life data from the DPV registry from Germany and Austria.
*Diabetes Res Clin Pract.* 2016; 115: 31-8
(IF=3.639)


225. Use of insulin pump therapy in children and adolescents with type 1 diabetes and its impact on metabolic control: comparison of results from three large, transatlantic paediatric registries. Diabetologia. 2016; 59(1): 87-91 (IF=6.08)


235. Type 1 diabetes mellitus. BMBF Competence Network Diabetes mellitus (IF=0.429)

Hansmann G, Miera O

Lopus H, Kuehne T, Beerbaum P, Apitz C, Hansmann G, Muthurangu V, Moledina S

Apitz C, Hansmann G, Schranz D

Hansmann G, Apitz C

236. Pulmonary hypertension associated with acute or chronic lung diseases in the preterm and term neonate and infant. The European Paediatric Pulmonary Vascular Disease Network, endorsed by ISHLT and DGPK. Heart. 2016; 102 Suppl: ii49-56 (IF=6.059)
Hilgendorff A, Apitz C, Bonnet D, Hansmann G

Kaestner M, Schranz D, Warnecke G, Apitz C, Hansmann G, Miera O


Lammers AE, Apitz C, Zartner P, Hager A, Dubowy KO, Hansmann G

Latus H, Kuehne T, Beerbaum P, Apitz C, Hansmann G, Muthurangu V, Moledina S


Udink Ten Cate FE, Hannes T, Germund I, Khalil M, Huntgeburth M, Apitz C, Brockmeier K, Schraudt A, Schraun M


244. MCM3AP and POMP Mutations Cause a DNA-Repair and DNA-Damage-Signaling Defect in an Immunodeficient Child. Hum Mutat. 2016; 37(3): 257-68 (IF=4.601)

Baraban E, Chavakis T, Hamilton BS, Sales S, Wabitsch M, Bornstein SR, Ehrhart-Bornstein M

Fabricius D, Trzaska T, Jahrsdörfer B

Hansmann G, Apitz C


Jahrsdörfer B, Panitz V, Fabricius D

Apitz C

256. [Current Guidelines to Prevent Obesity in Childhood and Adolescence]. Klin Padiatr. 2016; 228(1): 1-10 (IF=0.731)

Waltz M, Nusser S, Schmid MB, Dreyhaupt J, Reister F, Hummler H

258. Diabetes in Patients with β-thalassemia or other Hemoglobinopathies - Analysis from the DPV Database. Klin Padiatr. 2016; 228(6-07): 307-312 (IF=0.731)

Latus H, Schranz D, Apitz C

260. Pre-BCR signaling in precursor B-cell acute lymphoblastic leukemia regulates PI3K/AKT, FOXO1 and MYC, and can be targeted by SYK inhibition. Leukemia. 2016; 30(6): 1246-54 (IF=11.702)


266. Microbiological screening in preterm infants. Results and consequences for hygiene management. *Monatsschr Kinderheilkd.* 2016; 164(9): 805-812 (IF=0.31).

Lindner W, Essig A, Humllinger HD, Reister F, von Baum H.


Moss A, Sievert K, Siegfried W, Siegfried A, Brentii S, Koening W, Wabinitsch M.


Karpeit-Massler G, Ramani D, Shu C, Halatsch ME, Westhoff MA, Bruce IN, Canoll P, Siegelin MD.


Karpeit-Massler G, Banu MA, Shu C, Halatsch ME, Westhoff MA, Bruce IN, Canoll P, Siegelin MD.


277. 20 Years of Pediatric Benchmarking in Germany and Austria: Age-Dependent Analysis of Longitudinal Follow-Up in 63,967 Children and Adolescents with Type 1 Diabetes. *PLoS ONE.* 2016; 11(8): e0160971 (IF=2.806).


284. Therapeutic potential of the dual peroxisome proliferator activated receptor (PPAR)α/γ agonist aleglitazar in attenuating TNF-α-mediated inflammation and insulin resistance in human adipocytes. 


Massaro M, Scoditti E, Pellegrino M, Carluccio MA, Calabrìso N, Wabitsch M, Storelli C, Wright M, De Caterina R

285. Synkopen im Kindesalter

*Pädi Praktische Pädiatrie.* 2016; 2016(5): 276-282

Kaeßter M, Bride P, Apitz C

286. Vaccination of immunosuppressed children and adolescents

*Pädiatr Prax.* 2016; 85(3): 363-384

Schleker T, Speth F, Posovszky P


288. MRI-Based Liver Iron Content Determination at 3T in Regularly Transfused Patients by Signal Intensity Ratio Using an Alternative Analysis Approach Based on R2* Theory.

*Rofo.* 2016; 188(9): 846-52 (IF=1.418)

Wunderlich AP, Cario H, Bommer M, Beer M, Schmidt SA, Juchems MS

289. Noninvasive MRI-Based Liver Iron Quantification: Methodic Approaches, Practical Applicability and Significance.

*Rofo.* 2016; 188(11): 1031-1036 (IF=1.418)

Wunderlich AP, Cario H, Juchems MS, Beer M, Schmidt SA

290. miR-146a-mediated suppression of the inflammatory response in human adipocytes.


291. Ancillary therapies to enhance success of non-invasive modes of respiratory support - Approaches to delivery room use of surfactant and caffeine?

*Intrafamilial associations of cardiometabolic risk factors--results of the Ulm Birth Cohort Study.*

*Atherosclerosis.* 2015; 240(1): 174-83 (IF=3.942)

Brandt S, Moß A, Koenig W, Rothenbacher D, Brenner H, Wabitsch M

292. Subclinical and clinical hypothyroidism and non-alcoholic fatty liver disease: a cross-sectional study of a random population sample aged 18 to 65 years.

*BMC Endocr Disord.* 2015; 15: 41 (IF=1.739)


293. Intestinal epithelial cells promote secretion of leptin and adiponecin in adipocytes.

*Biochem Biophys Res Commun.* 2015; 458(2): 362-8 (IF=3.33)


294. [The Wolf-Hirschhorn Syndrome].

*Z Geburtshilfe Neonatol.* 2016; 220(5): 195-199 (IF=0.476)


2015

295. Hepatitis B Postexposure Prophylaxis in Preterm and Low-Birth-Weight Infants.


Wolz M, Hopfner R, Hummler HD, Heininger U

296. Ambulante, multidisziplinäre Adipositastherapie für Kinder und Jugendliche in der Regelversorgung. Die Ulmer Erfahrung

*Adipositas.* 2015; 9(1): 26-33

Denzer C, Weyhrer R, Wabitsch M

297. Leptin – Neuigkeiten von einem alten Bekannten

*Adipositas.* 2015; 9(3): 140-145

Funcke JB, Wabitsch M, Fischer-Posovszky P

298. Gegen Diskriminierung und für die Förderung von Kindern und Jugendlichen mit Adipositas – die Geschichte der AGA

*Aktuel Ernährungsmed.* 2015; 40(01): 50-53

Wabitsch M

299. Blood pressure in 57,915 pediatric patients who are overweight or obese based on five reference systems.


300. Intrafamilial associations of cardiometabolic risk factors--results of the Ulm Birth Cohort Study.

*Atherosclerosis.* 2015; 2016(5): 276-282

Brandt S, Moß A, Koenig W, Rothenbacher D, Brenner H, Wabitsch M

301. Intestinal epithelial cells promote secretion of leptin and adiponecin in adipocytes.


*Blood.* 2015; 125(22): 3420-31 (IF=11.847)

304. In vitro-generated MDSCs prevent murine GVHD by inducing type 2 T cells without disabling antitumor cytotoxicity.

**Blood.** 2015; 126(9): 1138-48 (IF=11.847)
Messemann JJ, Reisser T, Leithäuser F, Lutz MB, Debatin KM, Strauss G

305. First characterization of platelet secretion defect in patients with familial hemophagocytic lymphohistiocytosis type 3 (FHL-3).

**Blood.** 2015; 125(2): 412-4 (IF=11.847)


**Br J Haematol.** 2015; 170(4): 586-8 (IF=5.812)
Mcmullin MF, Bento C, Rossi C, Rainey MG, Girodon F, Cario H


**Cell Death Differ.** 2015; 22(1): 58-73 (IF=8.218)

308. Bariatrisch-chirurgische Eingriffe bei Jugendlichen mit extremer Adipositas

**Chirurg.** 2015; 105(S 02): S152-S157 (IF=0.466)

309. Clinical Practice Guideline: The Prevention and Treatment of Obesity [author reply to comments].

**Dtsch Arztebl Int.** 2015; 112(14): 250 (IF=3.738)
Wirth A, Wabitsch M, Hauner H

310. Treatment of young patients with HNF1A mutations (HNF1A-MODY).

Meissner T, Wölfe J, Scheuing N, Holl RW, DPV initiative the German BMBF Competence Network Diabetes Mellitus


**Diabetes Care.** 2015; 38(8): 1536-43 (IF=8.934)

312. Rates of diabetic ketoacidosis: international comparison with 49,859 pediatric patients with type 1 diabetes from England, Wales, the U.S., Austria, and Germany.

**Diabetes Care.** 2015; 38(10): 1876-82 (IF=8.934)

313. Accuracy of blood glucose meters for self-monitoring affects glucose control and hypoglycemia rate in children and adolescents with type 1 diabetes.

**Diabetes Technol Ther.** 2015; 17(4): 275-82 (IF=2.198)

314. Prävention und Therapie der Adipositas

**Diabetologie und Stoffwechsel.** 2015; 10(5 02): S152-S157 (IF=0.466)

315. Antifungal prophylaxis with posaconazole vs. fluconazole or itraconazole in pediatric patients with type 1 diabetes.

**Diabetologia** 2015; 58(8): 1536-43 (IF=8.934)

316. Treatment of young patients with HNF1A mutations (HNF1A-MODY).


**Diabetes Care.** 2015; 38(8): 1536-43 (IF=8.934)

318. Rates of diabetic ketoacidosis: international comparison with 49,859 pediatric patients with type 1 diabetes from England, Wales, the U.S., Austria, and Germany.

**Diabetes Care.** 2015; 38(10): 1876-82 (IF=8.934)

319. Accuracy of blood glucose meters for self-monitoring affects glucose control and hypoglycemia rate in children and adolescents with type 1 diabetes.

**Diabetes Technol Ther.** 2015; 17(4): 275-82 (IF=2.198)

320. Prävention und Therapie der Adipositas

**Diabetologie und Stoffwechsel.** 2015; 10(5 02): S152-S157 (IF=0.466)

321. Antifungal prophylaxis with posaconazole vs. fluconazole or itraconazole in pediatric patients with neutropenia.


322. TNF-related apoptosis-inducing ligand promotes human preadipocyte proliferation via ERK1/2 activation.

**FASEB J.** 2015; 29(7): 3065-75 (IF=5.299)
Funcke JB, Zoller V, El Hay MA, Debatin KM, Wabitsch M, Fischer-Posovszky P

323. Heart Rate Variability is Related to Disease Severity in Children and Young Adults with Pulmonary Hypertension.

**Front Pediatr.** 2015; 3: 63
319. Obesity and inflammation: reduced cytokine expression due to resveratrol in a human in vitro model of inflamed adipose tissue.  
Front Pharmacol. 2015; 6: 79 (IF=4.418)  
Zagotta J, Dimova EY, Debatin KM, Wabitsch M, Kietzmann T, Fischer-Posovszky P

Growth Horm IGF Res. 2015; 25(3): 115-20 (IF=1.448)  

321. Levothyroxine Treatment of Euthyroid Children with Autoimmune Hashimoto Thyroiditis: Results of a Multicenter, Randomized, Controlled Trial.  
Horm Res Paediatr. 2015; 84(4): 266-74 (IF=1.661)  

Horm Res Paediatr. 2015; 83(1): 1-10 (IF=1.661)  
Posovszky C, Wabitsch M

Horm Res Paediatr. 2015; 83(1): 11-8 (IF=1.661)  
Posovszky C, Wabitsch M

324. RIST: A potent new combination therapy for glioblastoma.  
Int J Cancer. 2015; 136(4): E173-87 (IF=5.531)  

325. Ethnicity and cardiovascular risk factors: evaluation of 40 921 normal-weight, overweight or obese children and adolescents living in Central Europe.  

326. PRKDC mutations associated with immunodeficiency, granuloma, and autoimmune regulator-dependent autoimmunity.  

327. Multicenter experience in hematopoietic stem cell transplantation for serious complications of common variable immunodeficiency.  

J Cancer Res Clin Oncol. 2015; 141(6): 1089-94 (IF=3.141)  
Weiss M, Steinbach D, Zintl F, Beck J, Gruhn B

329. Head Injury in Children: Has a Change in Circumstances Caused an Increase in Treatment Numbers?  
J Child Neurol. 2015; 30(9): 1153-8 (IF=1.434)  

330. Regulation of Angiopoietin-Like Proteins (ANGPTLs) 3 and 8 by Insulin.  
J Clin Endocrinol Metab. 2015; 100(10): E1299-307 (IF=5.531)  

J Clin Endocrinol Metab. 2015; 100(10): 3603-6 (IF=5.531)  
Patni N, Alves C, von Schnurbein J, Wehr C, Tannin G, Rakheja D, Garg A

332. Severe Early-Onset Obesity Due to Bioactive Leptin Caused by a p.N103K Mutation in the Leptin Gene.  
J Clin Endocrinol Metab. 2015; 100(9): 3227-30 (IF=5.531)  
333. Broad-spectrum antibodies against self-antigens and cytokines in RAG deficiency.  
Walter JE, Rosen LB, Csomas K, Rosenberg JM,  
Palma P, Cancrini C, Capuder K, Condino-Neto A, Costa-Cardvalho BT, Oliveira JB, Roifman C, Buchbinder D,  
Kumanovics A, Franco JL, Niehues T, Schuetz C,  
Kuijpers T, Yee C, Chou J, Masaad MJ, Geha R, Uzel G,  
Gelman R, Holland SM, Recher M, Utz PJ, Browne SK,  
Notarangelo LD

Bader P, Kreyenberg H, Rossig C, Corbacioglu S, Rajagopal R,  
Schütt C, Lang P, Müller I, Albert MH, Willasch AM, Klingebiel TE, Peters C

Schulz A, Woessmann W, Poetschger U, Zimmermann M, Klinegeibl T, Peters C

336. Kindlin-3-mediated integrin adhesion is dispensable for quiescent but essential for activated hematopoietic stem cells.  

337. CD4+ T cell-derived IL-21 and deprivation of CD40 signaling favor the in vivo development of granulocyte B-expressing regulatory B cells in HIV patients.  

338. Efficacy and safety of triple combination therapy with artesunate-amoquinidine-methylene blue for falciparum malaria in children: a randomized controlled trial in burkina faso.  
J Infect Dis. 2015; 211(5): 689-97 (IF=6.344)  
Coulibaly B, Pritsch M, Bountogo M, Meissner PE,  
Mockenhaupt FP, Drakeley C, Bousema T, Müller O

339. Olanzapine inhibits proliferation, migration and anchorage-independent growth in human glioblastoma cell lines and enhances temozolomide’s antiproliferative effect.  
J Neurooncol. 2015; 122(1): 21-33 (IF=2.754)  
Karpel-Massler G, Kast RE, Westhoff M, Dwucet A,  
Welscher N, Nonnenmacher L, Hlavac M, Siegel MD,  
Wirz CR, Debatin K, Halatsch M

340. Lutein Leads to a Decrease of Factor D Secretion by Cultured Mature Human Adipocytes.  
Tian Y, Kijlstra A, Renes J, Wabitsch M, Webers CA,  
Berendschot TT

341. Glucocorticoids attenuate acute graft-versus-host disease by suppressing the cytotoxic capacity of CD8(+) T cells.  
J Pathol. 2015; 235(4): 646-55 (IF=7.381)  
Theiss-Suennemann J, Jörk K, Messmann JJ, Reichardt SD, Montes-Cobos E, Lünder F, Tuckermann JP, AWolf H,  
Dressel R, Gröne HJ, Strauß C, Reichardt HM

342. Obesity in Youth with Type 1 Diabetes in Germany, Austria, and the United States.  
J Pediatr. 2015; 167(3): 627-32.e1-4 (IF=3.89)  
DuBose SN, Hermann JM, Tamborlane WV, Beck RW,  
Dost A, DiMeglio LA, Schwab KO, Holl RW, Hofer SE,  
Maahs DM, Type 1 Diabetes Exchange Clinic Network and Diabetes Prospective Follow-up Registry

343. Comorbidity of type 1 diabetes and juvenile idiopathic arthritis.  
J Pediatr. 2015; 166(4): 930-5.e1-3 (IF=3.89)  
Herrmann G, Thon, Mönkemöller K, Lilienthal E,  
Klinkert C, Holder M, Hörtchenhuber T, Vogel-Gerlicher P,  

J Pediatr. 2015; 167(2): 486-8 (IF=3.89)  
Yoshimi A, Strahm B, Niemeyer CM, Schulz A

345. Effects of Automated Adjustment of the Inspired Oxygen on Fluctuations of Arterial and Regional Cerebral Tissue Oxygenation in Preterm Infants with Frequent Desaturations.  
J Pediatr. 2015; 166(2): 240-244.e1 (IF=3.89)  
Waltz M, Schmid MB, Fuchs H, Mendler MR, Dreyhaupt J, Hummler HD

347. Bosentan-induced Reduction in Cyclosporine-A Levels: A Rare Interaction in an Infant With Osteopetrosis and Severe Pulmonary Hypertension.  

348. Comprehensive molecular characterization of human adipocytes reveals a transient brown phenotype.  
J Transl Med. 2015; 13: 135 (IF=3.694)  

349. Consensus of German transplant centers on hematopoietic stem cell transplantation in Fanconi anemia.  
Klin Padiatr. 2015; 227(3): 157-65 (IF=0.98)  

350. The Cause of Acute Respiratory Failure Predicts the Outcome of Noninvasive Ventilation in Immunocompromised Children.  
Klin Padiatr. 2015; 227(6-07): 322-328 (IF=0.98)  

351. Permissive hypercapnia in extremely low birthweight infants (PHELBi): a randomised controlled multicentre trial.  
Lancet Respir Med. 2015; 3(7): 534-43 (IF=15.328)  

352. Inaktives Leptin und extremes Übergewicht: Einer seltenen Erkrankung auf der Spur.  
Monatsschr Kinderheilkd. 2015; 163(2): 110-111 (IF=1.565)  
Herbst SM, Schirmer S, Posovszky C, Jochum F, Rödl T, Schroeder JA, Barth TF, Hehr U, Meltzer M, Vermehren J

Malar J. 2015; 14(1): 527 (IF=3.079)  

354. Fructose Alters Intermediary Metabolism of Glucose in Human Adipocytes and Diverts Glucose to Serine Oxidation in the One-Carbon Cycle Energy Producing Pathway.  
Metabolites. 2015; 5(2): 364-85  
Varma V, Boros LG, Nolen GT, Chang CW, Wabitsch M, Beger RD, Kaput J

Metabolomics. 2015; 11(3): 529-544 (IF=3.661)  
Varma V, Boros LG, Nolen GT, Chang CW, Wabitsch M, Beger RD, Kaput J

356. The combination of the PARP inhibitor Rucaparib and 5FU is an effective strategy for treating Acute Leukemias.  
Mol Cancer Ther. 2015; 14(4): 889-98 (IF=5.579)  

357. Angiotensin II directly impairs adipogenic differentiation of human preadipose cells.  
Mol Cell Biochem. 2015; 406(1-2): 115-22 (IF=2.613)  
Palominos MM, Dünner NH, Wabitsch M, Rojas CV

358. Inhibition of adipogenic differentiation of human SGBS preadipocytes by androgen-regulated microRNA miR-375.  
Mol Cell Endocrinol. 2015; 414: 177-85 (IF=3.859)  
Kraus M, Greither T, Wenzel C, Bräuer-Hartmann D, Wabitsch M, Behre HM

359. Gene expression levels of Casein kinase 1 (CK1) isoforms are correlated to adiponectin levels in adipose tissue of morbid obese patients and site-specific phosphorylation mediated by CK1 influences multimerization of adiponectin.  

360. Taking the next step forward - Diagnosing inherited infantile cholestatic disorders with next generation sequencing.  
Herbst SM, Schirmer S, Posovszky C, Jochum F, Rödl T, Schroeder JA, Barth TF, Hehr U, Meltzer M, Vermehren J

361. Surveillance after oncological Diseases in Childhood- and Adolescence  
Monatsschr Kinderheilkd. 2015; 163(2): 108-109 (IF=0.341)  
Debatin KM

362. Endocrinological Follow-up after oncological Diseases in Childhood- and Adolescence  
Monatsschr Kinderheilkd. 2015; 163(2): 110-111 (IF=0.341)  
Denzer C, Wabitsch M

363. Disorders in pubertal development and fertility. Late effects of antineoplastic therapy in childhood and adolescence  
Monatsschr Kinderheilkd. 2015; 163(2): 126-134 (IF=0.341)  
Denzer C, Hauffa BP, Rohrer T, Bramswig HJ, Dorr HG
365. Global situation of child health. Current situation and view into the future
Monatsschr Kinderheilkd. 2015; 163(11): 1110-1116
(IF=0.341)
Weber MW, Schultz A, Meissner P, Carai S, Kruger C

366. Biologically inactive leptin and early-onset extreme obesity [author reply to comments].
Fischer-Posovszky P, Funcke JB, Wabitsch M

367. Biologically inactive leptin and early-onset extreme obesity

368. Factors influencing success of clinical genome sequencing across a broad spectrum of disorders.

369. Reliability of pulse oximetry during cardiopulmonary resuscitation in a piglet model of neonatal cardiac arrest.
Neonatology. 2015; 107(2): 113-9 (IF=2.754)
Hassan MA, Mendler M, Maurer M, Waizt M, Huang L, Hummller HD

370. Risk Indicators for Air Leaks in Preterm Infants Exposed to Restrictive Use of Endotracheal Intubation.
Neonatology. 2015; 108(1): 1-7 (IF=2.754)

Neonatology. 2015; 108(1): 73-80 (IF=2.754)

372. Cerebral Oxygenation during Intermittent Hypoxemia and Bradycardia in Preterm Infants.
Neonatology. 2015; 107(2): 137-146 (IF=2.754)
Schmid MB, Hopfner RJ, Lenhof S, Hummller HD, Fuchs H

373. The functional anatomy of motor imagery after subacute stroke.
NeuroRehabilitation. 2015; 36(3): 329-37 (IF=1.453)
Kraft E, Schaal MC, Lule D, König E, Scheidtmann K

374. Toll-like receptor 5 in obesity: The role of gut microbiota and adipose tissue inflammation.
Obesity (Silver Spring). 2015; 23(3): 581-90 (IF=3.614)

375. MFAP5 is related to obesity-associated adipose tissue and extracellular matrix remodeling and inflammation.
Obesity (Silver Spring). 2015; 23(7): 1371-8 (IF=3.614)

376. Targeting of hyperactivated mTOR signaling in high-risk acute lymphoblastic leukemia in a pre-clinical model.
Oncotarget. 2015; 6(3): 1382-95 (IF=5.008)

Oncotarget. 2015; 6(16): 14507-21 (IF=5.008)

378. TIC10/ONC201 synergizes with Bcl-2/Bcl-xl inhibition in glioblastoma by suppression of Mcl-1 and its binding partners in vitro and in vivo.
Oncotarget. 2015; 6(34): 36452-61 (IF=5.008)

379. Additive regulation of adiponectin expression by the mediterranean diet olive oil components oleic Acid and hydroxytyrosol in human adipocytes.
381. A Potential Role for the Inhibition of PI3K Signaling in Glioblastoma Therapy. 

382. A new mutation in the KINDLIN-3 gene ablates integrin-dependent leukocyte, platelet, and osteoclast function in a patient with leukocyte adhesion deficiency-III. 
Pediatr Blood Cancer. 2015; 62(9): 1677-9 (IF=2.634) 
Crazzolara R, Maurer K, Schulz E, Zieger B, Zustin J, Schulz AS

383. Current use of metformin in addition to insulin in pediatric patients with type 1 diabetes mellitus: an analysis based on a large diabetes registry in Germany and Austria. 
Pediatri Diabetes. 2015; 16(7): S29-37 (IF=3.488) 

384. Depression, metabolic control, and antidepressant medication in young patients with type 1 diabetes. 

385. Sonographically measured suprailiac adipose tissue is a useful predictor of non-alcoholic fatty liver disease in obese children and adolescents. 
Pediatri Obes. 2015; 10(4): 260-6 (IF=3.488) 
Schlieske C, Denzer C, Wabitsch M, Oeztuerk S, Mason RA, Thieme D, Kratzer W

386. Schwindel in der Pädiatrie 
Bode H

Sex Dev. 2015; 9(3): 136-43 (IF=2.164) 

388. Sustained Aeration of Infant Lungs (SAIL) trial: study protocol for a randomized controlled trial. 
Trials. 2015; 16: 95 (IF=1.859) 

389. Endocrine and Metabolic Effects of Adipose Tissue in Children and Adolescents 
Zdr Varst. 2015; 54(2): 131-138 (IF=0.203) 
Kotnik P, Fischer-Posovszky P, Wabitsch M

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