Research Report 2011-2014
Department of Pediatrics and Adolescent Medicine
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## Imprint

**Publisher**  
Prof. Dr. Klaus-Michael Debatin, Director  
Department of Pediatrics and Adolescent Medicine, Ulm University

**Editor and Design:**  
Nicolas Marschall, Research Management

**Contents and Photos:**  
Cover picture: Gabriele Stautner; Research profile: Heiko Grandel;  
Other photos and illustrations: the respective researchers.

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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, which was the pioneer of interdisciplinary 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.

Our department participates in currently two Collaborative Research Centers (SFB) of the German Research Foundation (DFG) of Ulm University with Prof. Debatin as Co-Chair of the SFB 1074 “Experimental Models and Clinical Translation in Leukemia”.

With this report, we inform you about the focuses and developments during the last five 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 study the molecular mechanisms which, for example, lead to the emergence of neuroblastoma from progenitor and stem cells.

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 heirs of several forms of severe combined immune defects (SCID). In the late sixties one of the first ever bone marrow transplants in Europe was performed at our hospital. Novel therapies, such as haploidentical stem cell transplantations, cell-based immunotherapies and, most recently, radio immunotherapy-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 coordinates its focus on severe combined immune defects as part of the federal network on primary immunodeficiencies.

The Pediatric Endocrinology and Diabetes Section aims to elucidate the molecular causes of endocrine and metabolic diseases by focusing on monogenetic forms of obesity, special forms of diabetes mellitus and rare adipose tissue disorders such as lipodystrophy. Furthermore, we study the causes and effects of obesity in childhood and adolescence and develop novel therapy strategies. The BMBF-supported federal network on juvenile extreme obesity is coordinated by us. Our experimental research concentrates on the biology of adipose tissue. We develop in vitro model systems for studying human fat cell functions. For example, the human SGBS preadipocyte cell strain was generated in our lab and is now used in more than 200 research laboratories worldwide. Current projects involve the endocrine function of fat cells and the regulation of adipose tissue homeostasis through cellular mechanisms such as apoptosis. Furthermore, we characterize the function of newly discovered obesity genes within the framework of the National Genome Research Network (NGFN).

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.

Photos: Heiko Grandel
Research Groups

Apoptosis and Cancer Therapy

Heads: Prof. Klaus-Michael Debatin, Dr. Mike-Andrew Westhoff

Our work is focused on understanding mechanisms of sensitivity and resistance of tumor cells towards anticancer therapy. This includes the analysis of signaling pathways that may help to overcome resistance to molecular targeted therapy or conventional therapy using cytotoxic drugs and irradiation in human tumors with a particular focus on glioblastoma multiforme. Thus, our current work is directed at modulating signaling pathways (PI3-kinase, NF-kappaB) in glioblastoma tumor cell lines and primary ex vivo culture tumor cells to elucidate two key aspects of glioblastoma multiforme tumor biology:

- **Identification of alterations in key signaling pathways**

  Identifying proteins which are either mutated or exhibit altered expression in GBM and to further understand their role in the various signalling networks. This is of particular interest, as these proteins are frequently involved in multiple, partially overlapping signalling cascades, and thus their individual contributions to a given pathway is often difficult to identify. We aim to better understand the basic tumor biology and this should give us powerful tools to predict the behavior of GBM subtypes with respect to proliferation, invasion/metastasis and response to treatment. Furthermore, we thus hope to also identify novel potential targets for therapeutic intervention.

- **Novel therapeutic approaches**

  The current trend in treatment of cancer has moved towards metronomic therapy, whereby lower doses of drugs are given continuously or at frequent intervals, with the aim of reducing cytotoxic side-effects and increasing treatment efficacy. In close cooperation with the doctors treating patients at our clinic, we constantly work at improving existing treatment protocols and at identifying novel promising approaches. One such approach is the so-called combination therapy, whereby individual pharmacological inhibitors of cell signalling (sensitizers) are combined with low doses of more conventional chemotherapy to enhance tumor-specific apoptosis (programmed cell death), while concomitantly reducing side-effects. Recently, we have successfully expanded this idea further to the complex combination therapy, where several sensitizers are given in an optimized temporal sequence.
Experimental Pediatric Oncology Section

Head: Prof. Dr. Christian Beltinger

We concentrate on two research areas. In our focus “Pathogenesis of Embryonic Tumors” we investigate the interaction of oncogenes with tumor suppressors and enhancers in cells of origin and stem cells of embryonic tumors, in particular neuroblastoma.

Our second focus “Experimental Cancer Therapy” aims at developing novel preclinical strategies utilizing small molecules and genetic or viral cytotoxic effectors.

The molecular analysis of apoptosis and other cell death modes plays an important role in both research foci.

### Focus “Pathogenesis of Embryonic Tumors”

Neuroblastoma, an embryonic tumor, is the most common extracranial solid tumor in childhood. The aggressiveness of neuroblastoma is determined in part by the amplification of MYCN. MYCN both promotes and suppresses growth of neuroblastoma. The tumor-suppressive (e.g. proapoptotic) or tumor-promoting (e.g. antiapoptotic) mechanisms that have to be inactivated or activated, respectively, in neuroblastoma for MYCN to preferentially exert its oncogenic action remain an enigma. We therefore investigate the interaction of MYCN with dysfunctional tumor suppressors and activated oncogenes in the genesis, progression and aerobic glycolysis (Warburg effect) of neuroblastoma.

We isolate and characterize cells of origin and stem cells of neuroblastoma and other embryonic tumors. Our activities in this field are integrated into the research consortium “Tumor Stem Cells” of the Deutsche Krebshilfe (German Cancer Aid), which we coordinate.

### Focus “Experimental Cancer Therapy”

Specificity and efficiency are major obstacles in targeted tumor therapy. We develop novel approaches to overcome these hurdles. To this end we investigate small molecules that intervene specifically in signaling pathways crucial for survival of pediatric tumors. In addition, we test oncolytic measles virus and anti-cancer gene therapies. Analysis and modulation of apoptosis or cell lysis induced by these experimental therapies are integral parts of this focus.

Photo: Peripheral sympathetic progenitors (green), potential cells of origin of neuroblastoma and its stem cells.
Leukemia

Head: PD Dr. Lüder-Hinrich Meyer, Prof. Dr. Klaus-Michael Debatin

The main research interests of the Leukemia group are focussed on acute lymphoblastic leukemia (ALL), the most common malignant disease in childhood and adolescence. The aims of our work are to characterize and understand leukemia biology in order to develop novel treatment strategies comprising novel markers for risk stratification and new therapeutic approaches and substances including preclinical validation in an in vivo model system.

By combining comprehensive molecular and functional analyses we were able to identify leukemia-specific biological characteristics, which could serve as possible starting points for new therapies for high-risk leukemia. In order to evaluate these new therapy options preclinically, we have established a xenograft leukemia model that mimics the disease of the patient and thus allows to investigate the effectivity of new agents. With this model we have provided evidence for a good efficacy of several substances alone and in combination with conventional chemotherapy against high-risk ALL. In additional projects we are currently developing test procedures in order to identify the patients which can profit from a new form of therapy, with the aim to realize clinical application in a next step.

Immunoregulation and GVHD

Head: PD Dr. Gudrun Strauß

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 receptors 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.

**Obesity and adipose tissue biology – experimental and clinical studies**

Heads: Prof. Dr. Martin Wabitsch, PD Dr. Pamela Fischer-Posovszky

Obesity is a worldwide growing epidemic. The accumulation of fat tissue can lead to severe co-morbidities such as insulin resistance, type 2 diabetes mellitus, liver steatosis, and cardiovascular disease. Many underlying causes have been described with the heritability of body weight ranging between 40 to 70%.

The Pediatric Endocrinology and Diabetes Section is a center for monogenetic forms of obesity. We identified new mutations leading to congenital leptin deficiency. Affected patients are treated with human recombinant leptin (Metreleptin) leading to rapid normalization of body weight.

The experimental research at the Pediatric Endocrinology and Diabetes Section centers on adipose tissue. The number of fat cells is determined in childhood and remains constant for the rest of the life. Yet adipose tissue is a dynamic organ with about 10 percent of fat cells being replaced every year. Our group investigates the role of programmed cell death (apoptosis) in this remodeling process. Obesity is associated with an accumulation of macrophages into adipose tissue preceding the development of insulin resistance. We have shown that apoptotic fat cells attract macrophages to adipose tissue and that these immune cells interact with fat cells and cause insulin resistance. The vision of our research was to find a way to eliminate excessive fat cells by apoptosis. Based on our results we now think it may be more reasonable to prevent the apoptosis of fat cells subsequently preventing the infiltration of macrophages. In more recent projects we study the non-apoptotic functions of death ligands and death receptors in human fat cells.
Immunology, Regulation of dendritic cells

Head: PD Dr. Dorit Fabricius

### Regulation of interferon-α and granzyme B in human plasmacytoid dendritic cells

Plasmacytoid dendritic cells (pDC) are crucial mediators of innate and adaptive immune responses. A better understanding of pDC regulation may improve immunotherapeutic approaches to cancer, infectious diseases and autoimmunity. Apart from production of IFN-alpha and TNF-alpha we showed that pDC can secrete large amounts of the serine protease granzyme B (GrB), but no perforin. In the last years we investigated the regulation of GrB in pDC based on our finding that pDC-GrB effectively suppresses T cell proliferation. While the cytokines IL-3 and IL-10 played a key role for GrB induction, toll-like-receptor agonists and CD40 ligand inhibit GrB secretion. To characterize the physiological function of pDC-GrB, we explored the effect of commonly used antiviral vaccines on pDC and found that particularly TBEV vaccine was able not only to induce marked IFN-alpha secretion, but also to efficiently suppress pDC-derived GrB, which allowed for an efficient T cell response. PDC of healthy individuals after TBEV vaccination produced less GrB than before vaccination, a mechanism possibly contributing to a successful cellular immune response to the vaccine. Our data point to a potential involvement of GrB-secreting pDC in suppression of tumor-specific T cells and suggest that pDC can have a regulatory role, mediated by GrB in the absence of perforin; a mechanism that has also been described for regulatory T cells. Since IL-3 and IL-10 can also be found in the environment of malignant tissues, pDC-GrB may be involved in suppression of tumor-specific T cells. Interestingly TBEV was used in a tumor vaccination study as natural agonist and we assume that suppression of GrB contributed to the observed anti-tumor-effect. We intend to continue elucidating in more detail the role of pDC-derived GrB and intend to utilize an in-vitro culture model of immune responses against B cell leukemias. By including pDC from healthy subjects and from patients with B cell leukemias, we hope to achieve a better understanding of the role pDC play in health and disease and how this potent immunomodulating cell population may be manipulated therapeutically.

![Figure: Plasmacytoid dendritic cells incubated with Tickborn-encephalitis vaccine do not transfer Granzyme B to T cells anymore.](image)

### Immunogenisation of ALL cells as tumor vaccination approach

Acute lymphoblastic leukemia (ALL) is the most common pediatric malignancy. Although the vast majority of patients initially respond to chemotherapy, relapses occur in approximately 20% of cases and have a poor prognosis. Thus, novel therapeutic strategies are required to treat minimal residual disease and improve long-term survival. B cell precursor (BCP)-ALL cells express low levels of costimulatory and antigen-presenting molecules and therefore are poorly recognized by the immune system. Previous reports show that CpG oligodeoxynucleotides (CpG) can induce immunogenicity of non-Hodgkin’s lymphomas including B-CLL and in certain B cell leukemias. In our study on the effect of various combinations of known potent B cell
stimulators including CpG, interleukin (IL)-2 family cytokines and CD40 ligand (CD40L) on the immunogenicity of BCP-ALL cells we could show that the combination of CpG, IL-4 and CD40L was not only able to enhance expression of costimulatory and antigen-presenting molecules on BCP-ALL cells, but also enabled BCP-ALL cells to induce proliferative T cell responses and to generate cytotoxic T cells (CTLs). Of note, these CTLs exhibited significantly enhanced anti-leukemic cytotoxicity not only towards treated but also towards untreated BCP-ALL cells. Untreated control BCP-ALL cells induced only minimal T cell proliferation and cytotoxicity even in an allogeneic setting. Our results demonstrate that combined treatment with CpG, IL-2 family cytokines and CD40L is more efficient than CpG alone in inducing an immunogenic phenotype in BCP-ALL cells. In vitro CTL generation shall now be further optimized by additional stimulation of tumor-lysate-loaded activated pDC and the role of pDC in anti-leukemic immunity shall be further characterized. Apart from in vitro studies we will utilize a humanized leukemia mouse model that will be transplanted with BCP-ALL. In this xenotransplantation model we will test the anti-leukemic immune response of beforehand in vitro generated specific CTL. The planned in vivo study may provide novel insights in mechanisms of immunogenization and contribute to the development of immunotherapeutic vaccination approaches in the management of therapy-resistant BCP-ALL.

Social Pediatric Center and Child Neurology Section

Head: Prof. Dr. Harald Bode

- **Long-chain polyunsaturated fatty acids and ADHD**
  Investigators: Dr. Katharina Widenhorn-Müller, PhD (TransferCenter for Neuroscience and Learning), Prof. Dr. Harald Bode

In a randomized placebo-controlled intervention trial with 95 children 6-12 years of age with ADHD, the supplementation with long-chain polyunsaturated fatty acids increased the concentration of the fatty acids in erythrocyte membranes and improved working memory function, compared to the control group.

- **Long-term outcome at age 7-10 years or premature babies born before the 25th week of pregnancy**
  Investigators: Dr. Susanne Herber-Jonat (Neonatology, Hospital of the Ludwig-Maximilians-University Munich), Prof. Dr. Harald Bode

Of 79 originally very small premature babies, 76 showed no or mild motoric or intellectual impairment. The gestational age was no risk factor for frequency or severity of the impairment. Many children showed difficulties at school, behavioral problems and a long-term need for coaching.

- **Psychic trauma in children with cerebral palsy and spina bifida**
  Investigators: Dipl. Psych. Katy Kohleis, Prof. Markus Storck (Ostfalia University of Applied Sciences, Suderburg), Prof. Dr. Harald Bode

The multicentric study with 355 children and adolescents with cerebral palsy and spina bifida displayed more frequent emotional and behavioral problems as in a reference sample. The health-related quality of life was rated as lower. Familial stress was rated higher in children with cerebral palsy. Emotional and behavioral problems have a negative influence on the quality of life and thus are important starting points for interventions.
■ Inclusion of children with learning disabilities and handicaps in regular schools

Investigators: cand. med. Viola Hirner, Prof. Dr. Harald Bode

Parents of 209 preschool and school children expressed different experiences and expectations concerning the school of their children. They partly wished for special needs schools, partly for integrative regular schools. Many parents experienced anguish and problems prior to the choice of a school. The severity of disability was rated similar by parents and by professionals. In spite of a rather similar assessment of the degree of the child’s disability, there was only a moderate relation between the wish of the parents and the recommendation of the professionals from the social pediatrics center concerning the desired type of school. In line with the sociopolitical development towards more integration, the pedagogic and social-pedagogic advice needs to be intensified.

Non-malignant hematological diseases

Head: 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; D. Neumann, Tel Aviv), there are furthermore functional analyses of the potential pathogenetic role of the identified mutations.

■ Polycythemia vera in childhood and adolescence

As part of an international cooperation we collected clinical and molecular genetic data of eight pediatric patients with polycythemia vera, which is the largest cohort so far that was analyzed systematically and published in literature. The analysis of this data and of other published cases revealed several characteristics specific to pediatric patients with polycythemia vera, as well as insights into the molecular changes.

■ 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: Prof. Dr. Ansgar Schulz; Investigators: PD Dr. Manfred Hönig, Dr. Catharina Schütz

- **Primary Immunodeficiencies**

  Through our long lasting experience with diagnosis and therapy of primary immunodeficiencies – particularly stem cell transplantations 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 Section

Head: Prof. Dr. Helmut Hummler

■ 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 and an international consortium coordinated by the University of Miami, USA.

Currently we participate in two large international studies (SAIL-Trial, Presox-Trial) with special focus on delivery room care. Furthermore, we are working together with Stephan Medizin-technik GmbH with the aim to improve non-invasive respiratory support of newborns. These studies are funded by the Federal Ministry of Economic Affairs and Energy.

Additional studies are supervised by Dr. Schmid and primarily target cerebral oxygenization and with fluctuations of arterial and regional cerebral tissue oxygenation, and with the tissue oxygen saturation of various other organs.

■ 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: Dr. Carsten Posovszky

We perform single- and multi-center clinical studies in Pediatric Gastroenterology. For example, we assess the immunization status in children with inflammatory bowel disease and autoimmune hepatitis and evaluate effectiveness of varicella immunization under immunosuppressive therapy in a multi-center trial.

In addition, we conduct an abdominal pain interventional multi-center study funded by the German Research Foundation (DFG) to improve treatment of children 7-12 years of age with functional abdominal pain (FAP) and evaluate the diagnostic criteria for this entity.

Our basic research focuses on the cellular and molecular pathogenesis of congenital entero pathies. We recently elucidated pathomechanisms involved in the gastrointestinal manifestations found in in Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED) and Familial Hemophagocytic Lymphohistiocytosis (FHL) Type 5.
Large Collaborative Research Projects Coordinated

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

**Speaker:** Prof. Dr. Klaus-Michael Debatin  
**Head:** Prof. Dr. Christian Beltinger  
**Funding:** German Research Foundation (DFG)  
**Duration:** 2006-2014  
**Partners:** Several Institutes and Departments of Ulm University, see below

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

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

**Speakers:** Prof. Dr. Klaus-Michael Debatin, Prof. Dr. Simone Fulda  
**Funding:** Federal Ministry for Education and Research (BMBF)  
**Duration:** 2007-2013  
**Partners:** Goethe University Frankfurt, BioSolutions Halle GmbH

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

Research Consortium “Tumor Stem Cells”

Speaker: Prof. Dr. Christian Beltinger
Funding: German Cancer Aid (Deutsche Krebshilfe)
Duration: 2005-2013
Partners: German Cancer Research Center Heidelberg, Heinrich-Pette-Institute Hamburg, University of Regensburg, University of Cologne, University Hospital Bonn, University of Würzburg, Technical University of Munich, Institute of Molecular Medicine at Ulm University

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

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

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

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

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

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

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

■ GSC 270: International Graduate School in Molecular Medicine Ulm (IGradU)
  Faculty from our department: Prof. Dr. Christian Beltinger, Prof. Dr. Klaus-Michael Debatin, PD Dr. Pamela Fischer-Posovszky, PD Dr. Lüder H. Meyer, PD 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: 2007-2017
  Partners: Additional Departments and Institutes of Ulm University

■ Collaborative Research Center 1149: Danger Response, Disturbance Factors and Regenerative Potential after Acute Trauma
  Subproject Role of myeloid-derived suppressor cells in trauma (PD Dr. Gudrun Strauß)
  Subproject Role of severe obesity in healing of muscle injuries (Prof. Dr. Uwe Knippschild, Prof. Dr. Martin Wabitsch)
  Coordinator: Prof. Dr. Florian Gebhard, Dept. of Orthopaedic Trauma, Hand, Plastic, and Reconstruction Surgery
  Funding: German Research Foundation (DFG)
  Duration: 2015-2018
  Partners: Additional Departments and Institutes of Ulm University

■ Collaborative Research Center 1074: Experimental Models and Clinical Translation in Leukemia
  Subproject Attenuated oncolytic measles virus against ALL of childhood: preclinical proof-of-principle and molecular mechanisms (Prof. Dr. Christian Beltinger)
  Subproject The NOD/SCID/huALL xenotransplant model: characterization and prognostic impact of distinct engraftment properties (time to leukemia, TTL) of primary ALL cells (PD Dr. Lüder H. Meyer)
  Coordinator: Prof. Dr. Hartmut Döhner, Department of Internal Medicine III
  Vice Coordinator: Prof. Dr. Klaus-Michael Debatin
  Funding: German Research Foundation (DFG)
  Duration: 2012-2016
  Partners: Additional Departments and Institutes of Ulm University

■ Research Training Group GRK 1041: Molecular Diabetology and Endocrinology in Medicine
  Subproject Regulation of RBP4 in human fat cells and its role for adipose tissue inflammation and insulin resistance (Prof. Dr. Martin Wabitsch, PD Dr. Pamela Fischer-Posovszky)
  Coordinator: Prof. Dr. Bernhard Böhm, formerly Department of Internal Medicine I
  Funding: German Research Foundation (DFG)
  Duration: 2009-2012
  Partners: Additional Departments and Institutes of Ulm University
Boehringer Ingelheim Ulm University BioCenter (BIU)
Subproject *Regulation of proliferation, differentiation and function of human brown adipocytes* (Dr. Daniel Tews, PD Dr. Pamela Fischer-Posovszky, Prof. Dr. Martin Wabitsch)
Coordinator: Prof. Dr. Klaus-Michael Debatin (on behalf of the Medical Faculty)
Funding: State of Baden-Württemberg, Boehringer Ingelheim, Medical Faculty
Duration: 2011-2015
Partners: Groups from Ulm University and from Boehringer Ingelheim, Biberach

Else Kröner Research College Ulm – Stem cells, aging and malignant transformation
Fellows at our department: Dr. Melanie Schirmer, Dr. Felix Seyfried (Supervisors: Prof. Dr. Klaus-Michael Debatin, PD Dr. Lüder H. Meyer)
Coordinator: Prof. Dr. Stephan Stilgenbauer, Department of Internal Medicine III
Funding: Else Kröner-Fresenius Stiftung
Duration: 2012-2017
Partners: Additional Departments and Institutes of Ulm University

Preclinical Comprehensive Cancer Center (PCCC)
Work package *Preclinical models for AML and ALL* (Prof. Dr. Klaus-Michael Debatin, PD Dr. Lüder H. Meyer, Dr. S. Enzenmüller)
Coordinator: Prof. Dr. Hellmut Augustin, German Cancer Research Center, Heidelberg
Funding: Helmholtz Association
Duration: 2013-2016
Partners: Additional Departments and Institutes of Ulm University; Helmholtz Centers DKFZ, HMGU, MDC; EMBL, Max-Planck Institute for Brain Research, and the Universities of Heidelberg, Munich (TU) and Cologne

Life Course Approach to Obesity Research: From Epidemiology to Future Strategies of Prevention – EPI Germany
Subproject *Determinants and consequences of an excessive gain of body weight, waist circumference and body fat mass in specific phases of life in children and adolescents* (Prof. Dr. Martin Wabitsch, Dr. Stephanie Brandt)
Coordinators: Prof. Dr. Manfred J. Müller, University of Kiel
Prof. Dr. Heiner Boeing, German Institute of Human Nutrition
Funding: Federal Ministry for Education and Research (BMBF)
Duration: 2012-2015

Molecular Mechanisms of Adiposity
Subproject *Clinical Studies* and Subproject *Functional Studies* (Prof. Dr. Martin Wabitsch, PD Dr. Pamela Fischer-Posovszky)
Coordinator: Prof. Dr. Johannes Hebebrand, University of Duisburg-Essen
Funding: Federal Ministry for Education and Research (BMBF) – NGFNplus
Duration: 2008-2013
**Longitudinal Childhood Obesity Research in Germany (LARGE Consortium)**
- Subproject *Risk factors for overweight and obesity and their adverse metabolic consequences during childhood – Birth Cohort Study* (Prof. Dr. Martin Wabitsch)
  - Coordinator: Prof. Dr. Wieland Kiess, University of Leipzig
  - Funding: Federal Ministry for Education and Research (BMBF) Competence Network Adiposity
  - Dauer: 2008-2012

**miRNA – Novel markers to predict the development of obesity-related disorders?**
- Coordinators: PD Dr. Fischer-Posovszky, Prof. Dr. M. Wabitsch
- Funding: European Society for Paediatric Endocrinology (ESPE) Research Unit
- Grant Duration: 2013-2015
- Partners: Prof. Dr. Stefano Cianfarani, Prof. Dr. Nobili (University of Rome Tor Vergata)
  Dr. Primoz Kotnik, Prof. Dr. Tadej Battelino (University of Ljubljana)

**MPN&MPNr Euronet (COST Action)**
- 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)**
- 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

**German Network on Primary Immunodeficiency Diseases (pid.net)**
- Subproject *Genetics of human (severe) combined immunodeficiency (S)CID* (PD Dr. Manfred Höning)
  - Coordinator: Prof. Dr. Christoph Klein, Munich
  - Duration: Funded 2009-2012, network ongoing
  - Funding: Federal Ministry for Education and Research (BMBF)
  - Partners: Universities of Munich (LMU), Freiburg, Dresden, Berlin and Hannover

**OSTEOPETR: New Genes and Therapeutic Approaches to Osteopetrosis**
- Manager of the International registry of patients suffering from osteopetrosis: Prof. Dr. Ansgar Schulz
  - Coordinator: Dr. Alberto Giovanni Ugazio, Rome
  - Duration: ERA-NET funding received in 2007, registry ongoing
  - Partners: Universities of Paris, Hamburg and Berlin
  - Funding: ERA-Net for Research Programmes on Rare Diseases
Event Organization

2014

- **Boehringer Ingelheim Ulm University BioCenter (BIU) – 3rd Symposium**
  - Organizer: Prof. Dr. Klaus-Michael Debatin
  - Partner: Medical Faculty, Boehringer Ingelheim
  - Date, Venue: 07.03.2014, Ulm

- **50th Workshop for Pediatric Research**
  - Organizer: Prof. Dr. Klaus-Michael Debatin
  - Partner: German Society of Pediatrics and Adolescent Medicine (DGKJ)
  - Date, Venue: 20.-21.03.2014, Göttingen

- **Clinical Seminar: The Use of Oxygen, and Respiratory Pharmacotherapy**
  - Organizer: Prof. Dr. Helmut Hummler
  - Partner: IPOKRaTES Foundation
  - Date, Venue: 13.-15.03.2014, Ulm

- **Half-yearly symposium of the South German Pediatric Endocrinologists**
  - Organizers: Dr. Christian Denzer, Prof. Dr. Martin Wabitsch
  - Date, Venue: 22.02.2014, Ulm

- **7th Neuropediatrics Workshop**
  - Organizer: Prof. Dr. Harald Bode
  - Date, Venue: 11.01.2014, Ulm

2013

- **Advanced training course of the German speaking Society for Pediatric Gastroenterology and Nutrition**
  - Organizer: Dr. Carsten Posovszky, Dr. Christoph Schick
  - Partner: German speaking Society for Pediatric Gastroenterology and Nutrition
  - Date, Venue: 06.-08.11.2013, Bonn

- **49th Workshop for Pediatric Research**
  - Organizer: Prof. Dr. Klaus-Michael Debatin
  - Partner: German Society of Pediatrics and Adolescent Medicine (DGKJ)
  - Date, Venue: 12.-13.09.2013, Düsseldorf

- **Half-yearly symposium of the South German Pediatric Endocrinologists**
  - Organizers: Dr. Christian Denzer, Prof. Dr. Martin Wabitsch
  - Date, Venue: 06.07.2013, Ulm

- **16th Socialpediatric Afternoon**
  - Organizer: Prof. Dr. Harald Bode
  - Date, Venue: 12.06.2013, Ulm
Boehringer Ingelheim Ulm University BioCenter (BIU) – 2nd Symposium
Organizer: Prof. Dr. Klaus-Michael Debatin
Partner: Medical Faculty, Boehringer Ingelheim
Date, Venue: 03.06.2013, Ulm

Nutricia Allergy Academy Workshop
Organizer: Dr. Carsten Posovszky
Partner: Nutricia GmbH
Date, Venue: 26.04.2013, Ulm

2nd Symposium of Hematology Today: Rare Anemia
Organizer: Prof. Dr. Holger Cario
Partner: Dr. Stephan Lobitz (Charité, Berlin)
Date, Venue: 18.-20.04.2013, Stadthaus Ulm

Meeting of BMBF Network “Adolescents with Extreme Obesity”, YES-Study
Organizer: Prof. Dr. Martin Wabitsch
Partner: Federal Ministry for Education and Research (BMBF)
Date, Venue: 21.-22.02.2013, Ulm

2012

Symposium “Disorders of Sex Development”
Organizers: Prof. Dr. Martin Wabitsch, Dr. Clothilde Leriche
Partner: Network on Rare Diseases, Ulm University
Date, Venue: 07.12.2012, Ulm

48th Workshop for Pediatric Research
Organizer: Prof. Dr. Klaus-Michael Debatin
Partner: German Society of Pediatrics and Adolescent Medicine (DGKJ)
Date, Venue: 12.-13.09.2012, Hamburg

6th Neuropediatrics Workshop
Organizer: Prof. Dr. Harald Bode
Date, Venue: 27.06.2012, Ulm

Hematology and Oncology Retreat
Organizer: Prof. Dr. Christian Beltinger
Partner: International Graduate School in Molecular Medicine Ulm
Date, Venue: 22.-23.06.2012, Bregenz

Boehringer Ingelheim Ulm University BioCenter (BIU) Kick-Off Meeting and 1st Symposium
Organizer: Prof. Dr. Klaus-Michael Debatin
Partner: Medical Faculty, Boehringer Ingelheim
Date, Venue: 30.05.2012, Ulm
Event Organization

- **Half-yearly symposium of the South German Pediatric Endocrinologists**
  
  **Organizers:** Dr. Christian Denzer, Prof. Dr. Martin Wabitsch  
  **Date, Venue:** 31.03.2012, Ulm, and 15.12.2012, Ulm

- **German Competence Network Obesity, Kick-Off Meeting of 2nd Funding Period**
  
  **Organizer:** Prof. Dr. Martin Wabitsch  
  **Partner:** Federal Ministry for Education and Research (BMBF)  
  **Date, Venue:** 26.-27.03.2012, Ulm

- **Meeting of BMBF Network “Adolescents with Extreme Obesity”, YES-Study**
  
  **Organizer:** Prof. Dr. Martin Wabitsch  
  **Partner:** Federal Ministry for Education and Research (BMBF)  
  **Date, Venue:** 26.03.2012, Ulm

- **Training Event “The endocrinologic consultation”**
  
  **Organizer:** Prof. Dr. Martin Wabitsch  
  **Partner:** Ipsen company  
  **Date, Venue:** 17.-18.02.2012, Günzburg

**2011**

- **15th Socialpediatric Afternoon**
  
  **Organizer:** Prof. Dr. Harald Bode  
  **Date, Venue:** 06.07.2011, Ulm

- **Half-yearly symposium of the South German Pediatric Endocrinologists**
  
  **Organizers:** Dr. Christian Denzer, Prof. Dr. Martin Wabitsch  
  **Date, Venue:** 19.03.2011, Ulm, and 22.10.2011, Ulm

- **47th Workshop for Pediatric Research**
  
  **Organizer:** Prof. Dr. Klaus-Michael Debatin  
  **Date, Venue:** 24.-25.02.2011, Göttingen
Prizes and Awards

2014

- **Dr. Andrea Kresz**
  Poster Prize for the poster *First experience in the use of carbon dioxide insufflation for pediatric colonoscopy*
  German speaking Society for Pediatric Gastroenterology and Nutrition

- **Joanna Meßmann**
  Research Stipend 2014+2015
  José Carreras Leukaemia Foundation

- **Verena Zoller**
  STEPS-Award 2014 Poster Prize
  German Society for Pediatric Endocrinology and Diabetology (DGKED)

2013

- **PD Dr. Pamela Fischer-Posovszky and Prof. Dr. Martin Wabitsch**
  ESPE Research Unit Grant Award
  European Society for Paediatric Endocrinology (ESPE)

- **PD Dr. Pamela Fischer-Posovszky**
  Travel Grant 2013 for the ESPE Joint Meeting, Milan
  Forum Wachsen

- **M.Sc. Jan-Bernd Funcke**
  Poster Prize for the poster *TRAIL (TNF-related apoptosis-inducing ligand) promotes human preadipocyte proliferation via ERK1/2 activation*
  German Adiposity Society (DAG)

- **Dr. Julia von Schnurbein**
  Leonard-Thompson Memorial Prize
  German Pediatric Diabetology Study Group (AGPD)

2012

- **Dr. Pamela Fischer-Posovszky**
  Jürgen-Bierich Prize 2012
  German Society for Pediatric Endocrinology and Diabetology (DGKED)

- **Dr. Julia von Schnurbein, Dr. Anja Moss, Dr. Stella Nagel, Prof. Dr. Klaus-Michael Debatin, Prof. Dr. Martin Wabitsch, et al.**
  Karger Prize 2013, for the publication *Leptin Substitution Results in the Induction of Menstrual Cycles in an Adolescent with Leptin Deficiency and Hypogonadotropic Hypogonadism, Horm Res Paediatr., 2012; 77(2):127-33.*
  European Society for Paediatric Endocrinology (ESPE)

- **Dr. Julia von Schnurbein**
  Leonard-Thompson Memorial Prize
  German Pediatric Diabetology Study Group (AGPD)

- **PD Dr. Manfred Hönig**
  Poster Prize
  European Society for Immunodeficiencies (ESID) 15th Biannual Meeting, Florence
Guest Scientists

2011

- **Prof. Dr. Klaus-Michael Debatin**
  - German Cancer Aid Prize 2011
  - German Cancer Aid

- **Prof. Dr. Klaus-Michael Debatin**
  - Career Award
  - European Cell Death Organization (ECDO)

- **Dr. Stephanie Brandt**
  - STEPS-Award 2011 Poster Prize
  - German Society for Pediatric Endocrinology and Diabetology (DGKED)

- **Dr. Pamela Fischer-Posovszky**
  - Research Award
  - German Adiposity Society (DAG)

- **Natalie Hartmann and team members of the Strauß Group**
  - Poster Prize for the poster: In vitro-established alloantigen-specific CD8+ CTLs mediate graft-versus-tumor activity in the absence of graft-versus-host disease
  - Association for Cancer Immunotherapy (CIMT) Meeting in Mainz

- **Dr. Lüder H. Meyer, Dr. Sarah M. Eckhoff**
  - Kind Philipp Prize 2010 for research in pediatric oncology
  - Society for Paediatric Oncology and Haematology (GPOH)

- **Dr. Michaela Keuper**
  - STEPS-Award 2010 Poster Prize for her poster: Obesity-associated macrophage infiltration in human adipose tissue is linked to apoptosis of fat cells
  - German Society for Pediatric Endocrinology and Diabetology (DGKED)

2014

- **Prof. Dr. Thomas Kietzmann**
  - Faculty of Biochemistry and Molecular Medicine, University of Oulu, Finland
  - July 2014

- **Dr. Huang Li**
  - Southeast University, Nanjing, China
  - 2011-2014

- **Dr. Mohammed Hassan**
  - Sohag University, Sohag, Egypt
  - 2012-2014

- **Ismaeli Elbeshlawi**
  - Egypt
  - November to December 2014

- **Mohab Ragab**
  - Egypt
  - December 2013 to February 2014

- **Olga Ovcarov**
  - May to August 2014

- **Maher Halak**
  - Syria
  - July to September 2014

- **Tobias Rieder**
  - January to March 2014

- **Johannes Müller**
  - August 2014

- **Christine Schwarz**
  - Medical Center Heidenheim
  - August 2014 to July 2015

- **Nicole Berens-Riha**
  - 2014

- **Thomas Franke**
  - 2014
Dr. Jaida Manzoor  
Childrens Hospital and Institute of Childhealth, Department of Endocrinology, Lahore, Pakistan  
November 2014

Dr. Saquib Mahmood  
Department of Human Genetics & Molecular Biology, University of Health and Sciences, Lahore, Pakistan  
November 2014

Chun Xu, M.Sc.  
China  
2014-2015

2012

Dr. Nele Gheldorf  
Nestlé Institute of Health Sciences SA, Lausanne, Schweiz  
November 2012

Meng Yang (Sunny) Xia  
McMaster University, Toronto, Kanada  
May to June 2012

Dr. Eija Pöllänen  
University of Jyväskylä, Finnland  
March 2012

Dr. Patrick Gonzalez  
Hôpitaux universitaires Paris-Sud 2011/2012

Dr. Georg Karpel-Massler  
Department of Neurosurgery, Ulm University 2011/2012

2013

Dr. Luca Trentin  
Università di Padova  
September 2011 to February 2014

Dr. Azahara Ruperez Cano  
University of Granada, Spanien  
April - July 2012; April - June 2013

Prof. Daniel Konrad  
University Children’s Hospital Zürich  
April 2013

Dr. Florian Kiefer  
Medical University of Vienna, Department of Internal Medicine III, Division of Endocrinology and Metabolism  
January 2013

Raghavendra Mysore  
Minerva Foundation Institute for Medical Research, Helsinki, Finnland  
January 2013

2011

Dr. Ez-Zoubir Amri  
Institute of Biology, Valrose, Université de Nice Sophia Antipolis 2011

Prof. Dr. Philipp Scherer  
Director of the Touchstone Center, UT Southwestern Medical Center, Dallas, Texas 2011

Dr. Carolina Biz Rodrigues Silva  
University of Sao Paulo, Brazil  
October 2010 to September 2011

Prof. Primož Kotnik  
Pediatric Endocrinology, University Children’s Hospital Ljubljana, University Medical Center Ljubljana, Slovenia  
September 2010 to August 2011
Doctorates Conferred
Dr. med. = MD;
Dr. rer. nat. / Dr. biol. hum. = PhD

2014

- Markus Herrmann, Dr. med.
  A model of reversible dasatinib resistance in c-KIT-mutated acute myeloid leukemia with t(8;21)

- Katrin Himpel, Dr. med.
  Evaluation of a transcutaneous bilirubinometer

- Nora Hipp, Dr. rer. nat. (Institute of Physiological Chemistry)
  Mechanisms of MYC-Induced Tumorigenesis

- Li Huang, Dr. med.
  Non-invasive Intermittent Mandatory Ventilation in Preterm Infants with RDS Immediately after Extubation – a Controlled Study on Synchronized Non-invasive Mechanical Ventilation and Review of the Literature

- Melanie Kohler, Dr. med.
  Link between maternal smoking habits during pregnancy and the filial BMI at the age of 8 years – Results from the Ulm Study

- Marc Robin Mendler, Dr. med.
  Influence of permissive hypercapnia on gas exchange, lung damage, and hemodynamics on laboratory animals with severe “Acute Respiratory Distress Syndrome (ARDS)"

- Elisa Parys, Dr. med.
  Pulmonary morbidity in very premature preterm infants when non-invasive first line treatment and respiration strategies are applied

- Nadja Rauh, Dr. med.
  Course of the hospitalizations of pregnant women with potential preterm delivery in the perinatal center of Ulm University Medical Center

- Julia Schoss, Dr. med.
  Non-invasive respiration for the treatment of respiratory failure in children with hemato-oncologic diseases or after stem cell transplantation

- Simone Serra, Dr. med.

2013

- Carmen Dorneburg, Dr. rer. nat.
  Notch in the molecular pathogenesis and therapy of neuroblastoma

- Stefanie Enzenmüller, Dr. rer. nat.
  PI3-Kinase inhibition primes cancer cells for lysosomotropic agents

- Viola Hirner, Dr. med.
  Children with learning disorders and disabilities in integrative schools or in special schools? Perception of parents and professionals

- Christian Jörg Huse, Dr. med.
  Frequency of methyphenidate prescriptions in children with a migratory background and conception of the elective course “Transcultural Medicine”

- Lisa Lehmann, Dr. med.
  Relations between the parental weight status, selected behavioural factors and the development of overweight and abdominal adiposity of the child – Results of the Ulm birth cohort
Nadine Muschel, Dr. med.
Influence of the prevention program URMEL-ICE on anthropometric parameters, intra-abdominal fat and cardiovascular risk factors

Benedikt Nußbaum, Dr. med.
Effects of commonly used antiviral vaccines on human plasmacytoid dendritic cells

Amelie Rieser, Dr. med.
Clinical relevance of sonographically determined intra-abdominal fat depots in school children from Ulm; Results of the URMEL-ICE Study

Ina Rupprecht, Dr. med.
The relation between psychopathologic abnormalities and eating habits under consideration of sex differences and BMI in children

Shobit Saxena, Dr. biol. hum.
Neural crest-derived sympathoadrenergic-like progenitors of the postnatal murine adrenal gland

Christina Schlieske, Dr. med.
Sonographic and anthropometric body fat parameters as predictors for metabolic syndrome and fatty liver disease in overweight children and adolescents

Katharina Seiter, Dr. med.
The relation between infantile body-mass-index and depression, behavioural abnormality, ADHS phenotype and impulsivity

Franziska Alff (Jena), Dr. rer. nat.
Prevention of excess weight and adiposity in childhood and adolescence

Davida Blasius, Dr. med.
Effects of medicinal and non-medicinal therapeutic interventions on the symptomatology and quality of life of children with ADHD – Results from a multicentric long-term study at six social pediatric centers in Baden-Württemberg

Stephanie Brandt, Dr. biol. hum.
Identification of early childhood and family factors associated with cardiovascular risk factors in pre-pubertal age

Ursula Doblanzki, Dr. med.
Influence of body weight on the left ventricular muscular mass under special consideration of body weight distribution – results of the URMEL-ICE Study –

Stefanie Dorn (geb. Geiger), Dr. med.
Perinatal asphyxia of full-term newborns – prognostic factors for the psychomotoric development and resulting actions

Simon Grewendorf, Dr. med.
Radioimmunotherapy-based conditioning as part of hematopoietic stem cell transplantation in children with malignant and non-malignant diseases

Stella Nagel, Dr. med.
Characterization of apoptosis resistance in human preadipocytes and adipocytes

Claudia Jennewein, Dr. rer. nat.
Identification of a new proapoptotic role of Nuclear Factor κB in death receptor- and drug induced apoptosis

Stefan Kammerl (München), Dr. med.
Insulin resistance as risk factor for cardiovascular diseases and tumors and their association with smoking and alcohol consumption
Doctorates Conferred

- **Susanne Moschner, Dr. med.**
  Investigation of the Immature Platelet Fraction (IPF) in pediatric patients with primary and secondary thrombocytopenia

- **Dorothee Müller, Dr. med.**
  Prevalence and risk factors for small for gestational age neonates – Investigations on a birth cohort of the Department of Gynecology and Obstetrics of Ulm University

- **Sophie Papcke-Bodet (Münster), Dr. med.**
  Conversion rate of the pathological glucose tolerance of type 2 diabetes mellitus in overweight children and adolescents

- **Veronika Reisinger, Dr. med.**
  Relevance of NOD2 gene polymorphisms in pediatric and adult patients with chronic inflammatory bowel diseases for disease activity, bone density and therapy

- **Dirk Rosentreter, Dr. biol. hum.**
  CD95-resistance in long-term-activated cytotoxic T lymphocytes

- **Annemarie Schlitter, Dr. med.**
  CD57high neuroblastoma cells have characteristics of tumor-initiating cells

- **Dominic Stadel, Dr. rer. nat.**
  Targeting IAPs in pancreatic cancer therapy

- **Liane Wagner, Dr. rer. nat.**
  Smac mimetic sensitizes glioblastoma cells to Temozolomide-induced apoptosis in a RIP1- and NF-κB-dependent manner independently of TNFα

- **Benedikt Winter, Dr. med.**
  Epidemiological and socio-medical aspects of tungiasis in northeastern Brazil

2011

- **Annette Bangert, Dr. rer. nat.**
  Sensitization of glioblastoma to TRAIL-induced apoptosis by histone deacetylase inhibitors

- **Kerstin Hammer-Röll, Dr. med.**
  Influence of a year-long school-based prevention program on anthropometric parameters, cardiovascular risk factors, left ventricular muscular mass and intima-media thickness – results of the URMEL-ICE study

- **Natalie Hartmann, Dr. rer. nat.**
  Role of apoptosis-resistant T cells in allogeneic bone marrow transplantation

- **Sulamith Hefele, Dr. med.**
  Analysis of the influence of Ghrelin on the biology of the fat cell

- **Joachim Hepp, Dr. med.**
  The therapy with recombinant growth hormone and the effect in the initial year of treatment under special consideration of patients with growth hormone deficiency

- **Annemarie Huber, Dr. med.**
  Prevalence and risk factors for premature birth – Investigation on a birth cohort of the Department of Gynecology and Obstetrics of Ulm University from May 2007 to June 2008

- **Michaela Keuper, Dr. rer. nat.**
  The role of fat cell apoptosis during obesity-associated adipose tissue inflammation

- **Ivonne Naumann, Dr. rer. nat.**
  Bortezomib sensitizes neuroblastoma for TRAIL-induced apoptosis

- **Thomas Unterkircher, Dr. rer. nat.**
  Bortezomib-mediated sensitization for TRAIL-induced apoptosis in glioblastoma
Pengfei Xu, Dr. med.
Obesity and colorectal cancer: Gene expression analysis in omental adipose tissue and characterization of adiponectin specific regulation mechanisms

Lena Dietrich, Dr. med. dent.
Immunohistological biomarkers as gender-specific indicators of cellular senescence

Habiliations Conferred

2014

Dorit Fabricius, PD Dr. med.
Immune modulation of human plasmacytoid dendritic cells

2013

Pamela Fischer-Posovszky, PD Dr. rer. nat.
Regulation of adipose tissue homeostasis by adipocyte apoptosis
Subject: Experimental Medicine

Lüder H. Meyer, PD Dr. med.
Prognostic impact of leukemia biology in pediatric acute lymphoblastic leukemia

2011

Manfred Hönig, PD Dr. med.
The phenotypic variability of severe combined immunodeficiency (SCID): Basic principles and therapeutic consequences
Publications

Upcoming highlights in 2015

Biologically inactive leptin and early-onset extreme obesity.


2014

1. Interdisziplinäre Leitlinie der Qualität S3 zur „Prävention und Therapie der Adipositas“
*Adipositas.* 2014; 8(4): 179-221


2. Therapie der Adipositas in Deutschland. Möglichkeiten und Grenzen von der Diagnostik bis zur Kostenübernahme
*Adipositas.* 2014; 8(3): 119-125


*Adipositas.* 2014; 8(1): 5-11


4. Nachhaltige Wirkung eines Aktivitätssensors auf die Gewichtsabnahme im Rahmen eines strukturierten ambulanten Schulungsprogramms
*Adipositas.* 2014; 8(3): 126-136

Moss A, Wabitsch M

5. Artesunate Enhances the Antiproliferative Effect of Temozolomide on U87MG and A172 Glioblastoma Cell Lines.
*Anticancer Agents Med Chem.* 2014; 14(2): 313-8

(IF=2.939)


6. Phosphoinositide 3-kinases upregulate system xc(-) via eukaryotic initiation factor 2α and activating transcription factor 4 - A pathway active in glioblastomas and epilepsy.
*Antioxid Redox Signal.* 2014; 20(18): 2907-22

(If7.667)


7. Urticaria, fever, and hypofibrinogenemia.
*Arthritis Rheumatol.* 2014; 66(5): 1377

Mohr V, Schulz A, Lohse P, Schumann C, Debatin KM, Schuetz C

8. Unexpected plateauing of childhood obesity rates in developed countries.

Wabitsch M, Moss A, Kromeyer-Hauschild K

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Dieluweit U, Debatin KM, Grabow D, Kaatsch P, Peter R, Seitz DC, Goldbeck L
Sources of Funding

Without financial support from external sources, our research would not be possible.

We cordially thank all organizations and individuals supporting us, in particular:

- German Research Foundation (DFG), including the Excellence Initiative of the German Federal and State Governments
- German Federal Ministry for Education and Research (BMBF)
- European Union
- Ministry of Science, Research and the Arts Baden-Württemberg
- Helmholtz Association
- Local charities, in particular Förderkreis für tumor- und leukämiekranke Kinder Ulm e.V.
- Medical Faculty of Ulm University (intramural programs)
- German Cancer Aid
- Boehringer Ingelheim Ulm University BioCenter (BIU)
- Else Kröner-Fresenius Foundation
- Wilhelm Sander Foundation
- German José Carreras Leukaemia Foundation
- Baden-Württemberg Foundation
- European Society for Paediatric Endocrinology
- German Adiposity Society
- COST Association
- Brunhilde von Hornstein Foundation
- Jeffrey Modell Foundation
- Juvenile Adiposity Foundation
- Individual Donors
- Industry