

The Team:**Head of Department:** K-M. Debatin**Professors:** C. Beltinger, G. Lahr, M. Wabitsch**Group Leaders/Postdocs:** D. Fabricius, P. Fischer-Posovszky, L.H. Meyer, G. Strauss, M-A. Westhoff**PhD Students:** A. Bangert, A. Bender, S. Demir, C. Dorneburg, E. Enlund, S. Enzenmüller, N. Hartmann, N. Hasan, C. Jennewein, S. Karl, M. Keuper, V. Klinkosch, S. Löder, I. Mader, J.J. Meßmann, I. Naumann, S. Saxena, D. Stadel, T. Unterkircher, K. Vellanki, L. Wagner, I. Zagotta, V. Zoller**Study Programme Experimental Medicine Students:**

R. Blosssey, L. Breckerbohm, L. Christner, S. Hasslacher, M. Herrmann, M. Linn, B. Mandel, S. Nagel, B. Nussbaum, V. Panitz, J. Philipp, V. Schwar, F. Seyfried, S. Stroh, J. Stursberg, S. Ulrich, F. Zirngibl

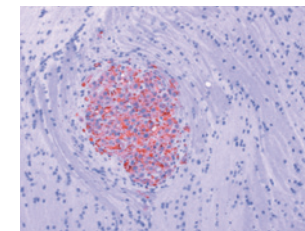
Additional Members of Thesis Advisory Committees:

P. Agostinis (Leuven), B. Baumann (Ulm), A. Bürkle (Konstanz), C. Classen (Rostock), C. Friesen (Ulm), S. Fulda (Frankfurt), I. Jeremias (Neuherberg), H.A. Kestler (Ulm), T. Kietzmann (Oulu), P. Lovat (Newcastle), M. Lutz (Würzburg), O. Micheau (Dijon), T. Seufferlein (Ulm), S. Stilgenbauer (Ulm), G. te Kronnie (Padua), I. Wernstedt Asterholm (Dallas), L. Wiesmüller (Ulm), R. Zwacka (Galway)

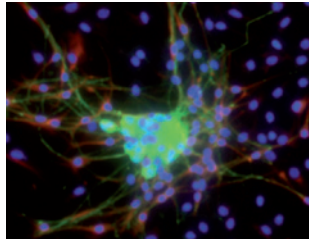
**Department of Pediatrics and Adolescent Medicine****Apoptosis and Cancer Therapy****Heads:** Prof. Dr. Klaus-Michael Debatin, Dr. Mike-Andrew Westhoff

The aim of our group is to understand how malignancies develop resistance to common cancer therapies and are thus able to avoid apoptosis and other forms of cell death.

We made key contributions to translational cell death research and have successfully developed combination approaches, whereby conventional therapy is paired with novel pharmacological substances that allow for the use of reduced amounts of chemotherapeutics, and thus reduced side effects, without the loss of potency, while concurrently enhancing tumor-specificity. Many of these approaches are currently being evaluated in vivo or are already being transferred to a clinical setting.



Microscopic section of a human Glioma growing in a mouse brain. Note the invasive phenotype which common in vivo approximations are unable to recapitulate.



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

Pathogenesis and Experimental Therapy of Pediatric Tumors

Head: Prof. Dr. Christian Beltinger

The Beltinger group investigates the pathogenesis of embryonic tumors and their stem cells and develops new preclinical therapies for these and other pediatric tumors. In the process, the molecular analysis of apoptosis and other types of cell death play an important role.

Leukemia

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

The main aims of our group are to characterize features of leukemia biology reflecting patient outcome and to identify novel therapeutic strategies. Employing a previously established xenograft leukemia model, we are investigating mechanisms of leukemia development in different organ compartments and functionally evaluating aberrant signaling in leukemia cells as a target for directed treatment of pediatric leukemia.

Immunoregulation and GVHD

Head: PD Dr. Gudrun Strauss

T cells are the mediators of the cellular immune response. They eliminate invading pathogens and protect from diseases but they can also turn their reactivity against self and induce either autoimmunity or the deleterious graft-versus host disease (GVHD), the main complication after allogeneic bone marrow transplantation. A prerequisite for both processes is the specific activation of T cells by the cognate antigen. Our work focuses on the role of death receptors in antigenic T cell activation and the development of new treatment strategies for GVHD by interfering with death receptor pathways or by using myeloid-derived suppressor cells.

Experimental Obesity Research

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

The excessive accumulation of adipose tissue in obesity leads to the development of severe co-morbidities such as type 2 diabetes mellitus and cardiovascular disease. Complementing our clinical studies in obese children and adolescents, our experimental research has centered on the biology and pathobiology of adipose tissue. Using a variety of molecular, cellular and in vivo approaches, we aim to understand the mechanisms controlling adipose tissue mass.

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Selected Publications:

- Keuper M, Wernstedt Asterholm I, Scherer PE, Westhoff MA, Möller P, Debatin K-M, Strauss G, Wabitsch M, Fischer-Posovszky P (2013): TRAIL (TNF-related apoptosis-inducing ligand) regulates adipocyte metabolism by caspase-mediated cleavage of PPARgamma. *Cell Death Dis.* 4:e474.
- Hartmann N, Messmann JJ, Leithäuser F, Weiswange M, Kluge M, Fricke H, Debatin KM, Strauss G (2013): Recombinant CD95-Fc (APG101) prevents graft-versus-host disease in mice without disabling antitumor cytotoxicity and T-cell functions. *Blood.* 121(3):556-65.
- Schlitter AM, Dornburg C, Barth TF, Wahl J, Schulte JH, Brüderlein S, Debatin K-M, Beltinger C (2012): CD57(high) neuroblastoma cells have aggressive attributes ex situ and an undifferentiated phenotype in patients. *PLoS One.* 7(8):e42025.
- Queudeville M, Seyfried F, Eckhoff SM, Trentin L, Ulrich S, Schirmer M, Debatin K-M, Meyer LH (2012): Rapid engraftment of human ALL in NOD/SCID mice involves deficient apoptosis signaling. *Cell Death Dis.* 3:e364.
- Meyer LH, Debatin K-M (2011): Diversity of human leukemia xenograft mouse models: implications for disease biology. *Cancer Res.* 71(23):7141-4.
- Hartmann N, Leithäuser F, Albers C, Duyster J, Möller P, Debatin K-M, Strauss G (2011): In vitro-established alloantigen-specific CD8+ CTLs mediate graft-versus-tumor activity in the absence of graft-versus-host disease. *Leukemia.* 25(5):848-55.