7th Student Symposium
on Molecular Medicine

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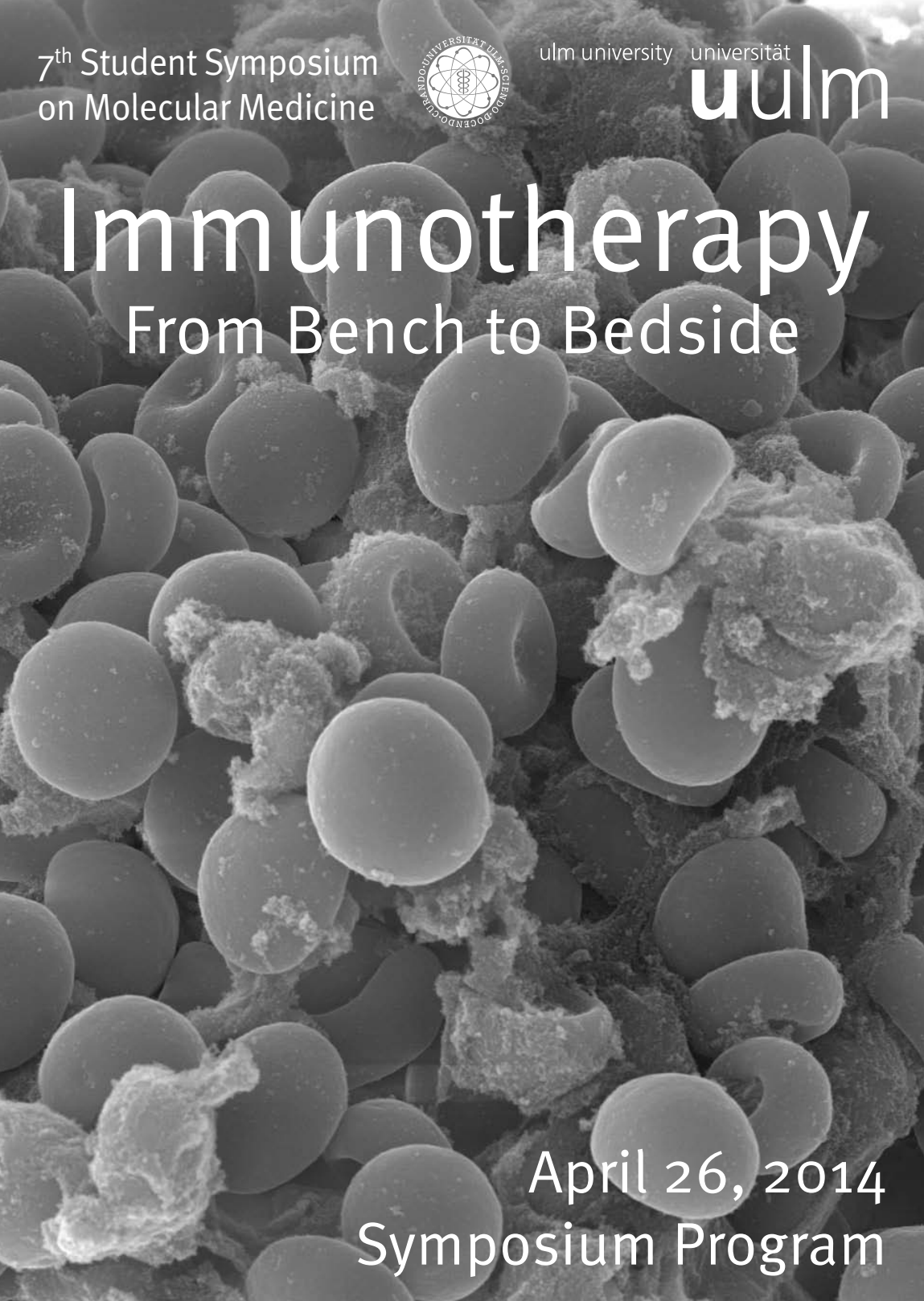
Immunotherapy

From Bench to Bedside



April 26, 2014
Symposium Program

Dear Symposium Participants,

it is a great pleasure to welcome you to the 7th Student Symposium on Molecular Medicine in the lovely town of Ulm.

Intriguing talks on current research in the field of immunotherapy await you. We are happy to welcome speakers from all over Germany. Their talks will cover a wide range of fields, including fundamental research in tumor immunotherapy, industrial production and development of antibodies as well as their clinical applications. Our speakers from universities, pharmaceutical companies and the clinic will provide us with a more comprehensive picture of immunotherapy. At this point, we would like to thank all the speakers who have joined us today, the sponsors and donors as well as the helpers that have made this event possible.

This event has come a long way in the past seven years. Starting as a platform to advertise our study course to the pharmaceutical industry, taking a short detour to inspire young students to commit to medical research, we now try to combine all these aspects by organizing a symposium for students by students.

For the first time this year, we are also giving students the opportunity to present their current research projects in a poster session.

Hopefully, you will have plenty of opportunity to engage our speakers and students in conversation while we are taking care of refreshments and food. As always we will provide you with coffee and a selection of our legendary homemade cakes.

We hope you will have an interesting and engaging day!

The Organization Committee

Symposium Program

9:00 - 9:10	Introduction	
9:15 - 10:00	Hassan Jumaa *Ulm*	B Cell Development and the Generation of Antibodies
10:00 - 10:45	Uwe Bücheler, *Biberach*	Biopharmaceuticals: Technology and Product Innovation - to Approach Unmet Clinical Need for Treatment of More Patients Worldwide
10:45 - 11:15	Coffee Break	
11:15 - 12:00	Vijay Rawat & Fabian Mohr, *Ulm*	Leukemia Stem Cells: Novel Target For Antibody Therapy
12:00 - 12:30	Stefan Stevanović *Tübingen*	Multiepitope Vaccines for Tumor Immunotherapy
12:30 - 12:45	Lea Prokop *Tübingen*	MultiPro: Immunogenicity Testing of Natural HLA Ligands
12:45 - 14:00	Lunch Break + Poster Session	
14:00 - 14:30	Student Representatives	Master Program and International Graduate School in Molecular Medicine
14:30 - 15:00	Antonio Pezzutto *Berlin*	Transgenic T Cells in the Therapy of Leukemia and Lymphoma
15:00 - 15:15	Sara Boiani *Berlin*	B Lineage-Specific TCR as Therapeutic Approach: Targeting CD79
15:15 - 15:45	Coffee Break	
15:45 - 16:30	Klaus Bosslet *Penzberg*	The Late Stage Pre-Clinical and Early Clinical Roche Oncology pRED Pipeline: Mode of Action, Pharmacology, and First Clinical Results
16-30 - 17:15	Martin Bommer *Ulm*	From Bench to Bedside - Clinical Applications of Monoclonal Antibodies

Abstracts and CVs

B Cell Development and the Generation of Antibodies

Prof. Dr. Hassan Jumaa

During B cell development, antibodies are assembled by random gene recombination to produce vast number of specificities. A potential risk of this process is that some of the antibodies produced are auto-reactive or poly-reactive. Traditional thoughts have mainly focused on how such putatively dangerous specificities are dealt with and in how they contribute to the development of autoimmune diseases. However, a positive or even necessary role of self-recognition during B cell development has rarely been taken into account.

To screen the potential auto-antigens of the auto/poly-reactive antibodies produced during the B cell development conventional assays such as ELISA, Hept2 slides or Protoarray have been used. These assays have several discrepancies between their in-vitro set up and the physiology of B cells. For instance, the antibodies to test are expressed as recombinant IgG isotype and the antigens used in the conventional assays are immobilized in a repetitive manner, while antigens can be in soluble form in-vivo. We introduced an alternative approach using a cell-based assay to measure antigen–binding to BCRs expressed on the cell surface and found that most of the antibodies, which were identified as auto/poly-reactive as soluble IgG in conventional assays, were not auto/poly-reactive when expressed as membrane-bound IgM BCR.

1992-1993	Diploma thesis at the Max-Planck-Institute of Immunobiology
1993-1997	Doctoral thesis at the Max-Planck-Institute of Immunobiology
1998-2001	Postdoctoral fellow, University of Freiburg and Max-Planck-Institute of Immunobiology
2005	Habilitation in Molecular Immunology, University of Freiburg
2010	Professor in Molecular Immunology, University of Freiburg
2001-2013	Group leader of Molecular Immunology, Max-Planck-Institute of Immunobiology and University of Freiburg, Germany
2013-	Director of the Institute of Immunology, Universitätsklinikum Ulm

Biopharmaceuticals: Technology and Product Innovation - to Approach Unmet Clinical Need for Treatment of More Patients Worldwide

Prof. Dr. Uwe Bücheler

Biopharmaceuticals is an emerging class of new drugs that do deliver new therapeutical options for treatment of more patients worldwide. These molecules are manufactured using living systems, were microbial and mammalian expression systems dominate. The primary route of application is parenteral which comes with high requirements for aseptic processing. Starting out with “natural compounds” e.g. Insulin or plasminogen activator the currently major class are monoclonal antibodies. Future molecule formats are “designed” natural structures like nanobodies or darpins open new areas of application. Manufacturing of consistent product profiles in global manufacturing networks is a special challenge for bio-pharmaceutical manufacturers.

1988 - 1989	Research fellow at Roche, Penzberg
1989 - 1991	Ph. D. in Molecular Biology at the University of Heidelberg
1991 - 2006	Various positions at Boehringer Ingelheim: Regulatory Affairs, Validation, CMC/GMP Documentation and Biological Safety, Quality Unit, Process Science
2006 - 2010	Site Head Boehringer Ingelheim Biberach
2010 -	SVP Global Biopharma Operations Boehringer Ingelheim
2013 -	interim SVP Biopharmaceuticals, responsible for the entire Biopharma business unit of Boehringer Ingelheim

Leukemia Stem Cells: Novel Target For Antibody Therapy

Jun.-Prof. Dr. Vijay Rawat

Rawat VPS et al. *The Vent-like homeobox gene VENTX2 promotes human myeloid differentiation in vitro and in vivo and is highly expressed in acute myeloid leukemia.* Proc Natl Acad Sci U S A. 2010

Rawat VPS et al. *Overexpression of CDX2 perturbs HOX gene expression in murine progenitors depending on its N-terminal domain and is closely correlated with deregulated HOX gene expression in human acute myeloid leukemia.* Blood. 2008

2000-2002	M.Sc in Analytical Biochemistry in AIC, Calcutta
2002-2006	Doctoral Thesis (Ph.D.), Ludwig-Maximilians University, Munich,
2005-2008	Postdoctoral fellow in Prof. Christian Buske's group, CCG Leukemia, Klinikum Grosshadern, LMU, Munich, Germany
2008-2009	Junior group leader in Prof. Christian Buske's group, CCG Leukemia, Klinikum Grosshadern, LMU, Munich, Germany
Since 2010	Junior Professor, Institute of Experimental Cancer Research, University Hospital Ulm

Fabian Mohr, MSc, PhD Student

F Mohr, K Döhner, C Buske, VPS Rawat. *TET genes: new players in DNA demethylation and important determinants for stemness*. Experimental hematology. 2011

09/2009	Bachelor of Science in Applied Biology, University of Applied Sciences Bonn-Rhein-Sieg Bachelor's Thesis at the Institute Anatomy and Cell Biology, UK Aachen
03/2012	Master of Science in Molecular Medicine, Ulm University Master's Thesis at the Institute for Experimental Cancer Research, Comprehensive Cancer Center & University Hospital Ulm
04/2012	PhD Student at the International Graduate School in Molecular Medicine, Ulm University / Institute for Experimental Cancer Research, Comprehensive Cancer Center & University Hospital Ulm

Multiepitope Vaccines for Tumor Immunotherapy

Prof. Dr. Stefan Stevanović

Selected Publications:

Dengjel J et al. *Autophagy promotes MHC class II presentation of peptides from intracellular source proteins*. Proc Natl Acad Sci U S A. 2005

Stoltze L et al. *Two new proteases in the MHC class I processing pathway.* Nat Immunol. 2000

Dick TP et al. *Coordinated dual cleavages induced by the proteasome regulator PA28 lead to dominant MHC ligands*. Cell. 1996

1980 –1988	Diploma Studies in biochemistry at the University of Tübingen
1988 – 1992	PhD thesis on Multiple Sequence Analysis at the Institute of Organic Chemistry, Tübingen
1992 – 1993	Postdoctoral research fellow in the laboratory of Hans-Georg Rammensee at the Max Planck Institute for Biology, Tübingen
1993 – 1996	Head of Laboratory at the Section of Tumor Virus Immunology, German Cancer Research Centre (DKFZ)
1996 – 2004	Group leader at the Department of Immunology, Interfaculty Institute for Cell Biology, University of Tübingen
2004 –	Head of the Section of Molecular Immunology, Department of Immunology, Interfaculty Institute for Cell Biology, University of Tübingen

MultiPro: Immunogenicity Testing of Natural HLA Ligands

Lea Prokop, PhD Student

Steinl C et al. *Release of matrix metalloproteinase-8 during physiological trafficking and induced mobilization of human hematopoietic stem cells*. Stem Cells Dev. 2013

Transgenic T Cells in the Therapy of Leukemia and Lymphoma

Prof. Dr. Antonio Pezzutto

Research Interests:

1) TCR gene transfer for the therapy of Leukemias and Lymphomas. T-cell receptors specifically recognizing EBV antigens or presented epitopes of the B-cell antigen CD22 and CD79 are being cloned for gene transfer in T-cells for adoptive T-cell therapy (cooperation with W. Uckert and Th. Blankenstein, MDC)

2) Tumor and Dendritic cell vaccination: a pilot study with a gene-modified tumor cell vaccine in renal cancer has been recently concluded as well as a phase I Dendritic cell vaccination in chronic myeloid leukemia. Follow-up studies are planned. DNA vaccination using vectors coding for cytokines or chemokines is being studied in animal models in cooperation with the MDC group of M. Lipp.

3) Generation of peptides mimicking antibody reactivity for construction of new immunotoxins based on internalization. Using an in –vitro evolutionary technique starting with a 10e17 peptides library we have selected several peptides reacting with the CD22 antigen. These might be potent tool for the construction of new immunotoxins (much cheaper than antibody pro¬duction, easy biochemical manipulation).

4) Clinical Studies in Lymphoma Therapy. We have strongly supported the use of radio¬immunotherapy in follicular Lymphoma and our results should be soon published in the Journal of Clinical Oncology (minor revisions requested). In Cooperation with C. Schmitt, G. Lenz and C. Scholz we have organized a Charité-wide Lymphoma study group and are planning to involve the city hospitals and the private practice Colleagues of Berlin into a cooperative study group on Lymphoma and Myeloma. New molecular targets such as PI3-Kinase, BTK etc. are in the focus of research. We plan to use molecular monitoring of therapy response by biopsy in selected lymphoma patients undergoing chemotherapy treatment.

1972-78	Study of Medicine, Univ. of Padua, Italy
1978	Doctoral Thesis at the Dept of Immunopathology, Univ. of Padua, Italy
1978-82	Residency, Univ. of Padua, Italy
1983-94	Residency & Attending in Internal Medicine, Univ. of Heidelberg.
1992	"Promotion", Univ. of Heidelberg: The B-cell reconstitution after autologous transplantation
1993-2001	Deputy Director, Dept of Hematology Oncology & Tumorimmunology, Rössle-Klinik, Charité Campus Buch, Berlin
1998-	Group Leader, Molecular Immuno-therapy, MDC Berlin
2001-2011	Deputy Director, Dept of Hematology Oncology, Charité Campus Virchow Klinikum
2011-	Director, Dept. of Hematology Oncology, Charité Campus Benjamin Franklin

B Lineage-Specific TCR as Therapeutic Approach: Targeting CD79

Sara Boiani, MSc, PhD Student

Cancer chemotherapies are the backbone of tumor treatment, but they present limitations due to toxicity, resistance and relapse. Recently TCR-gene therapy, using antigen-specific TCR-CD8+ T cells, has shown promising results in complete rejection of large tumors in mouse model and in the treatment of melanoma and synovial sarcoma. The homogeneity and easily accessibility make leukaemia and lymphomas suitable for this kind of therapy. 80% of them are derived from B cells, and tumor cells often conserve B-cell lineage-specific markers, such as CD79, a heterodimer α/β associated with BCR complex. The overall high incidence of CD79 expression in common B-cell neoplasms (95% CD79α- positive and 75% CD79β-positive) and its restriction to the B-cell lineage makes it attractive for a receptor-targeted immunotherapy. Moreover, due to the strictly lineage-specific expression of this antigen, we assume that off target effects should be less important compared to other tumor-associated antigens which have a broader tissue expression. Since CD79 belongs to the human self-antigen repertoire, endogenous T cells are tolerant to it. To overcome this obstacle, we use a mouse model (ABabDII) in which a chimeric human HLA-A2 (HHD) and the human TCR-α and-β chains (ABab construct) are transgenically expressed. We isolated reactive T cells after mice vaccination with human CD79, and after in vitro stimulation with a peptide library, we identified two antigen-specific TCR sequences, one for CD79α and one for CD79β. If the results of this preclinical study look promising, the future prospective will be to start a clinical trial.

2006-2009	Laurea (BSc) in Biotechnology at the University of Bologna, Italy
2009-2011	Laurea Magistrale (MSc) in Medical Biotechnology at the University of Bologna, Italy
2012	Volunteer Researcher at the Istituto Ramazzini - Cesare Maltoni Cancer Research Center, Bentivoglio, Italy
2012-2013	Science Assistant at the Babraham Institute, Cambridge, UK
2013-	PhD student at the Max-Delbrück Center for Molecular Medicine, Berlin

The Late Stage Pre-Clinical and Early Clinical Roche Oncology pRED Pipeline: Mode of Action, Pharmacology, and First Clinical Results

Dr. Klaus Bosslet

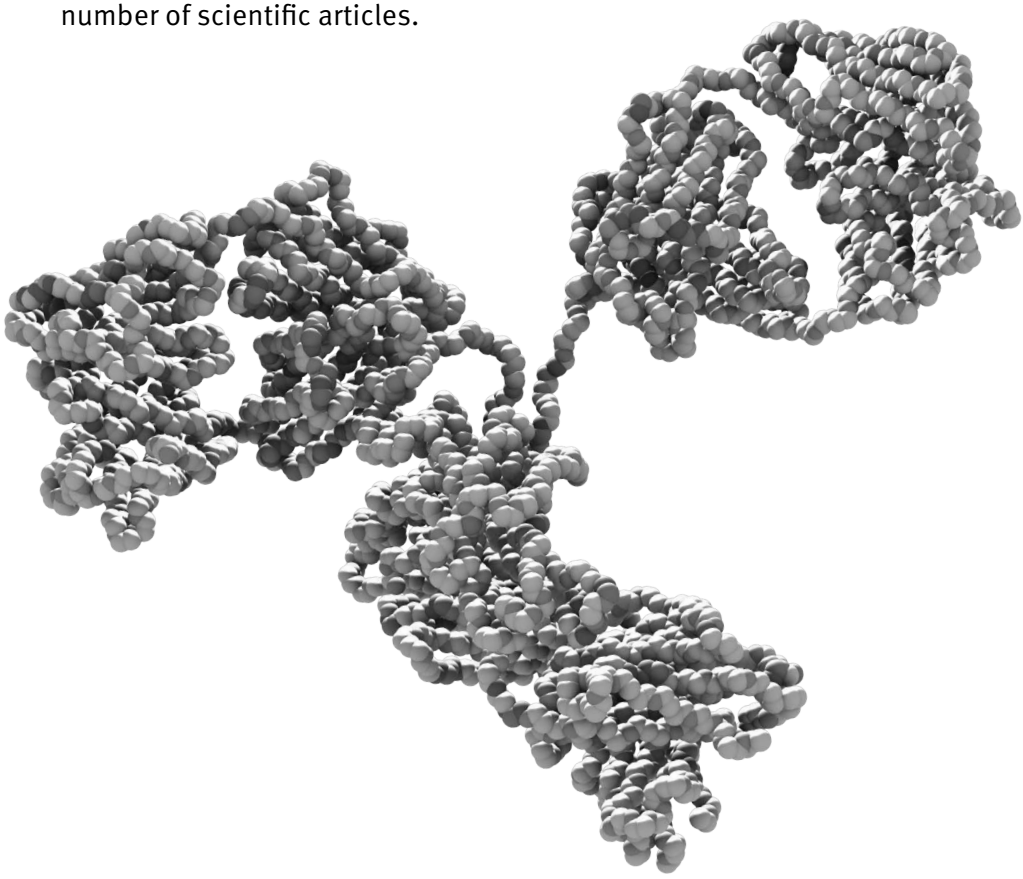
The early clinical development pipeline of Roche oncology contains targeted drugs which interfere with the physiological function of membrane targets such as CD20, CSF1R, Her3, Tie2, VEGFR etc. A short overview on the mode of action of antibody therapeutics interfering with these targets will be presented as well as first clinical efficacy signals.
Furthermore, the mode of action of a second class of compounds will be presented which uses tumor selective membrane targets to deliver toxic payloads which result in very strong efficacy signals in preclinical model systems. The payloads we are using differentiate from those of competitors in their potential to kill both quiescent as well as proliferating tumor cells resulting in increased efficacy signals compared to conventional antibody drug conjugates.
In summary, there is significant hope and excitement about the novel compounds which may help to prolong survival of cancer patients and potentially will cure.

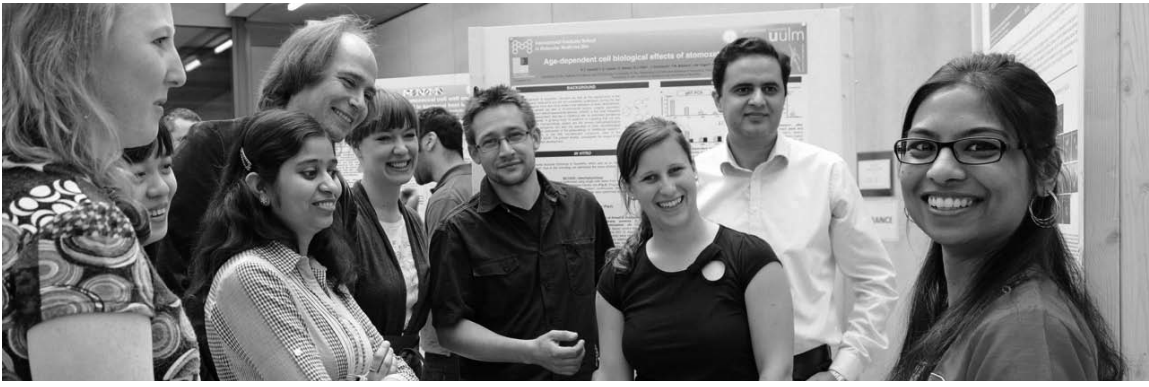
1980	PhD in Tumor-Immunology and Virology, University of Heidelberg
1980-1996	PostDoc at the DKFZ, Heidelberg and Behringwerke AG, Marbug
1996-1998	Director of R+D at ProVirus, Gaithersburg, USA
1998-2008	Head of the Dep. of Oncology Research and Global Head of Oncology Research at Schering AG, Berlin
2008-2011	Global VP Discovery Oncology at MedImmune, Cambridge, UK
2011-	Head of Discovery Oncology at Roche, Penzberg

From Bench to Bedside - Clinical Applications of Monoclonal Antibodies

Dr. Martin Bommer

Martin Bommer, MD is Head of Section for Infectious diseases and clinical immunology of the University of Ulm which is part of the department of Medicine III (Prof. Dr. H. Döhner). His research activities focus on leptomeningeal disease in lymphoma and leukemia including new diagnostic approaches as well as thrombotic microangiopathies (TMA). He is member of the center for rare diseases (Zentrum für seltene Erkrankungen) Ulm and is responsible for the clinical care of patients with rare anemia including clinical trials for the management of those patients. He serves as a reviewer of scientific journals and has published a number of scientific articles.





International PhD Programme in Molecular Medicine

Target group: MSc graduates
Number of places per year: unlimited
Application deadline: All year round
Length of programme: 3 years
Course language: English
Course content: Central element of the programme is the three-year doctoral dissertation in any field of molecular medicine at the end of which the student must defend his/her research results in a public disputation. Apart from their own laboratory work, doctoral students must attend compulsory courses amounting to 20 ECTS over a three-year period. These include, for example, series of lectures and seminars and practical laboratory training courses. In addition to curricular seminars and lectures a large variety of optional activities is offered. Two intermediate examinations during the three years' programme ensure appropriate progress in the student's scientific project.
Aim of the course: The major aim of the programme is to train graduates to be able to perform independent scientific research and to advance graduate career opportunities in the academic world and in industry.
Final degree: Doctor of Philosophy (PhD) or Doctor rerum naturalium (Dr. rer. nat.)

Fast Track PhD Programme in Molecular Medicine

Target group: Highly motivated and talented BSc graduates. After passing the first year examination of the Master's course of studies in Molecular Medicine, students with above-average results will be given the opportunity of directly entering the three-year doctoral phase.
Application deadline: Four weeks after passing the first year examination of the Master's course of studies.
Length of programme: 4 years
Course language: English
Course content: See Master course of studies and International PhD Programme
Aim of the course: See International PhD Programme in Molecular Medicine
Final degree: MSc/PhD

International Graduate School in Molecular Medicine Ulm

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Notes

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