Department of Infectious Diseases

Major Infectious Diseases

DEPARTMENT OF INFECTIOUS DISEASES, HEIDELBERG UNIVERSITY

Research Groups of the Department of Infectious Diseases

Infectious Diseases - A Brief Description

Studies of infectious diseases at the molecular and cellular level are a rather new research area, whose origin as an independent scientific discipline can be traced back to the discovery of microorganisms.

Even though infectious diseases have been known for thousands of years, exact knowledge of their source emerged only in the past century. Thus, the discovery of bacteria and viruses e.g. as cause for certain diseases began just in the middle of the 19th century.

Nowadays it is common knowledge that infectious diseases are caused by bacteria, viruses, fungi or parasites, and the rising threats from multiresistant bacteria or the emergence of new pathogens like influenza or SARS are frequently in the news. Apart from their enormous medical significance, however, microorganisms are important model systems for molecular and cell biology.

For example, RNA splicing was discovered in adenoviruses, oncogenes were found for the first time in retroviruses and the structure of nucleosomes was described primarily in DNA viruses.

Today, the science of infectious diseases is an interdisciplinary topic at the interface between medicine and molecular and cell biology. With this fact in mind, the newly created Major "Infectious Diseases" within the MSc "Molecular Biosciences" offers the opportunity to study this topic in considerable depth, both in theory and in practice.

Research at the Department of Infectious Diseases

The main research topics of the departments include HIV/Aids, malaria, viral hepatitis and the interaction between bacteria and host cells (immunology of infection). All departments are well integrated into different local and international research consortia and networks, some of which are coordinated by departments of the institute.

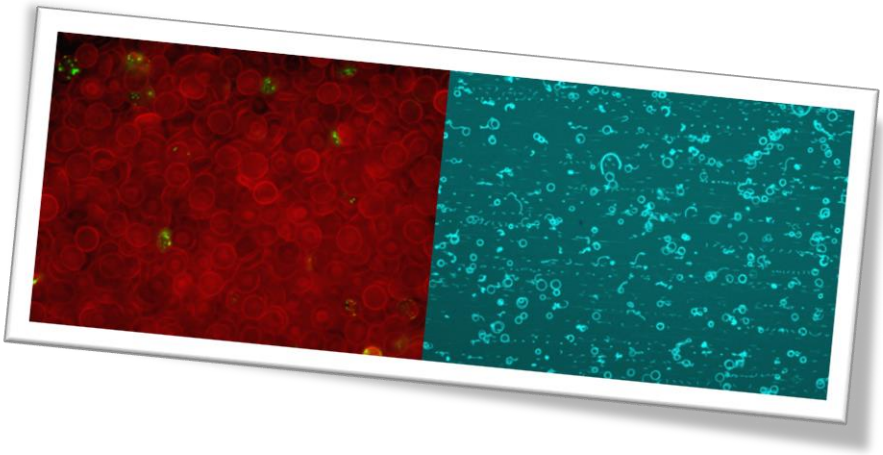
One example is the Cluster of excellence "CellNetworks". In addition there are close interactions and scientific cooperations with numerous institutions of Heidelberg University, the European Laboratory for Molecular Biology (EMBL), the German Cancer Research Center (DKFZ) and the Max-Planck-Institute for Medical Research. In addition, we collaborate with numerous institutions in Europe and beyond.

To find out more about the scientific research activities of the Department of Infectious Diseases, the ZMBH-group and the associated research groups participating in this Major, please look at the profiles, which are in the appendix and the corresponding websites.

The Department of Infectious Diseases aims to further extend and strengthen these research activities in particular by integrating interdisciplinary approaches and most recent technologies. These include high-resolution light and electron microscopy with the three-dimensional reconstruction of complex cellular structures, high through-put method screening for proteome and transcription analyses as well as time-resolved analysis of pathogen / host-cell interactions by using live cell imaging, mathematic modelling and simulation.

Content and Structure of the Major Infectious Diseases

The Major "Infectious Diseases" is intended for students with a good basic knowledge of molecular and cell biology who wish to put their main focus on infectious disease pathogens. In the context of the Major they will deepen their knowledge of the basics of molecular and cell biology and get to know specific aspects of the replication of infectious pathogens and their interactions with their hosts. The participating departments and research groups offer internationally renowned research programs as well as an excellent infrastructure and they are very well connected with other research institutions inside and outside the university. Therefore, they offer ideal conditions for the Major "Infectious Diseases".



Criteria for admission

We welcome appropriately qualified students from all over the world to this course. Modern infectious disease research focuses on molecular mechanisms of pathogenesis, so a good basic knowledge of molecular and cell biology is a prerequisite for admission. Some prior knowledge of infectious disease biology and immunology is also helpful, but not a prerequisite. Students in the Heidelberg Bachelor courses "Biology" and "Molecular and Cellular Biology" who are interested in this Major are advised to attend the lectures and courses on microbiology, infectious disease immunology, parasitology and virology in Semesters 4 and 5.

Acquired Degree

With the successful completion of the course the student acquires the MSc in Biology with the specialization (Major) "Infectious Diseases". This Master's degree qualifies students to enter PhD programs in Europe or could be a starting point for a career in the pharmaceutical industry or a biotech company.

Various doctoral study programs are offered by the institutes involved in the "Infectious Diseases" Major. Further information is to be found on the websites of the participating departments. Students who are particularly keen to pursue a doctoral degree, and who have sufficiently high grades, may transfer to a doctoral program already after three semesters of Masters studies.

CONTACT POINT

Major Infectious Diseases

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Education at the Department of Infectious Diseases

The department of Infectious Diseases at the Medical Faculty of Heidelberg represents the subject of Infectious Diseases in research, education and diagnostics, in the fields of bacteriology, virology, parasitology and public health. There are six units, most of which are involved in the educational activities of this Major. These units are:

- Medical Microbiology and Hygiene
- Molecular Virology
- Virology
- Integrative Virology
- Parasitology

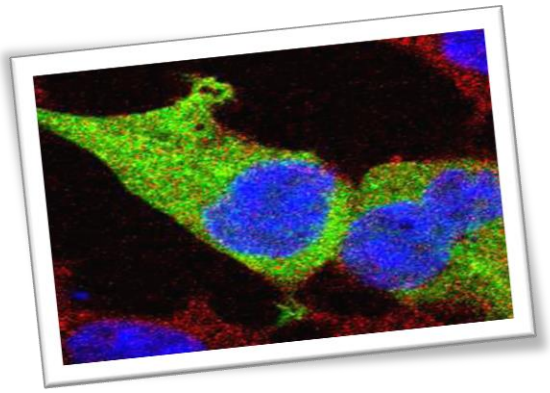
Most department heads are members of both the Faculty of Biosciences and the medical faculty and therefore are involved in teaching in both faculties. Previous lecture series and practicals in Biosciences, which were performed partially in collaboration with study groups at the Center for Molecular Biology Heidelberg (ZMBH) and the German Cancer Research Centre (DKFZ) were always well attended and dealt with molecular- and cell-biological aspects of medically important infectious diseases and their causative agents. Thus they covered an interdisciplinary field of high relevance. Detailed information regarding the contents of the individual lectures (e.g. collection of slides) can be found on the websites of the corresponding departments.

Medical Mircobiology

Fields of Interest

Teams in the Medical Microbiology and Hygiene department work in the field of Infection & Immunity. Specifically, we are interested to understand how host immunity reacts towards the contact with invading pathogens. A focus over the last years has been innate immunity which comprises the first line of defense against pathogenic microorganisms. Groups within the department study the biology of macrophages and dendritic cells which first encounter microbes. Moreover, frontline immunity at mucosal surfaces is analyzed. As the immune system is organized as a cellular network, communication between cells is of crucial importance. Therefore the department has a deep interest in signal transduction.

While classical bacteriology focuses on virulence factors and pathogenicity principles it is nowadays obvious that altered immune responses are equally important for infection susceptibility. The department analyzes the complex interplay of bacteria and immune cells thereby paving new roads for understanding current problems in infection defense, including sepsis, opportunistic infections in immunocompromised hosts and multi-resistant bacteria.



In order to address these topics we are using a multitude of methods and experimental approaches covering the fields of immunology, microbiology, molecular and cell biology as well as biochemistry.

The following teams belong to Medical Microbiology:

-Prof. Dr. Klaus Heeg (Head of the Medical Microbiology)

-Prof. Dr. Alexander Dalpke

-PD Dr. Katharina Hieke-Kubatzky

Prof. Dr. Alexander Dalpke

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Scientific Vita

Since 2013: PI, German Center for Lung Research (DZL), TLRC HD

2012-2015: Coordinator "Teaching and Education", German Center for Infection Research (DZIF HD)

2011: Consultant in microbiology, virology and epidemiology of infections

2008-2011: Speaker of the Postgraduate Program "Differential activation and integration of signaling modules within the immune system"

Since 2007: Member of "Hartmut Hoffmann-Berling International Graduate School of Molecular and Cellular Biology"

2006-present: Professor (W_3) for Medical Microbiology and Infection and Immunity

2006: Specialist in immunology ("Fachimmunologe DGfI", DGfI)

2004: Habilitation, University lecturer for infection and immunity; Topic: Suppressor of Cytokine Signaling (SOCS) proteins as regulators of the activity of the innate immune system

1999-2004: PostDoc and Research Assistant, Inst. of Medical Microbiology, Philipps-University Marburg

1998-1999: First-year resident, Kreis- und Stadtkrankenhaus Alfeld, Internal Medicine, License to practice medicin1998: Graduation (MD), Med. Microbiology, Center of Hygiene and Human Genetics, University Göttingen (summa cum laude)

1992-1998: Medical student, Georg-August University Göttingen

Specific Research Interests

- Infection & Immunity
- Innate immunity, pattern recognition receptors
- Mucosal immunology
- Cytokine signaling
- Immunostimulation through bacterial nucleic acids
- Immune functions of airway epithelium
- Suppressor of Cytokine Signaling proteins (SOCS)

Selected Publications

Eigenbrod T, Pelka K, Latz E, Kreikemeyer B and Dalpke AH: TLR8 Senses Bacterial RNA in Human Monocytes and Plays a Nonredundant Role for Recognition of Streptococcus pyogenes. **J Immunol 2015** Jun 22. pii: 1403173. [Epub ahead of print]

Weitnauer M, Schmidt L, Ng Kuet Leong N, Muenchau S, Lasitschka F, Eckstein V, Hübner S, Tuckermann J and Dalpke AH: Bronchial epithelial cells induce alternatively activated dendritic cells dependent on glucocorticoid receptor signaling. **J Immunol 2014;** 193(3): 1475-84

Hidmark A, von Saint Paul A, Dalpke AH: Cutting Edge: TLR13 is a receptor for bacterial RNA. **J Immunol 2012;** 189(6): 2717-21

Gehrig S, Eberle ME, Botschen F, Rimbach K, Eberle F, Eigenbrod T, Kaiser S, Holmes WM, Erdmann VA, Sprinzl M, Bec G, Keith G, Dalpke AH* and Helm M*: Identification of modifications in microbial, native tRNA that suppress immunostimulatory activity. **J Exp Med 2012**; 209(2): 225-233

Strebovsky J, Walker P, Lang R .and Dalpke AH: Suppressor of cytokine signaling 1 (SOCS1) limits NFκB signaling by decreasing p65 stability within the cell nucleus. **FASEB J 2011**; 25(3): 863-874

Peter ME, Kubarenko AV, Weber ANR, Dalpke AH: Identification of an N-terminal recognition site in TLR9 that contributes to CpG-DNA mediated receptor activation. **J Immunol 2009**; 182(12): 7690-7697

Baetz A, Koelsche C, Strebovsky J, Heeg K, Dalpke AH: Identification of a nuclear localization signal in suppressor of cytokine signaling 1 (SOCS1). **FASEB J 2008**; 22(12): 4296-4305

Bartz H, Avalos NM, Baetz A, Heeg K and Dalpke AH: Involvement of Suppressors of Cytokine Signaling in Toll-like receptor-mediated block of dendritic cell differentiation. **Blood 2006**; 108(13): 4102-4108

Zimmermann S, Murray PJ, Heeg K, Dalpke AH: Induction of Suppressor of Cytokine Signaling-1 (SOCS-1) by Toxoplasma gondii Contributes to Immune Evasion in Macrophages by Blocking IFN-gamma Signaling. **J Immunol 2006**; 176(3): 1840-1847

Bätz A, Frey M, Heeg K and Dalpke AH: Suppressor of cytokine signaling (SOCS) proteins indirectly regulate Toll-like receptor signaling in innate immune cells. **J Biol Chem 2004**; 279(52): 54708-54715

PD Dr. Katharina Hieke-Kubatzky

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Scientific Vita

2012: Habilitation in "Molecular Medicine" at the University of Heidelberg

2008: Max Kade Grant for a research year at the University of Michigan, Ann Arbor, USA

2007-present: Group Leader at the Department of Infectious Diseases, University of Heidelberg

2005-2006: Junior Group Leader at the University of Freiburg, Institute of Experimental and Clinical Pharmacology and Toxicology

2002-2004: Postdoctoral Fellow at the Ludwig Institute for Cancer Research, Brussels, Belgium

2001-2002: Researcher at Alantos Pharmaceuticals, Heidelberg

1997-2000: PhD Thesis at the Max Planck Institute for Immunobiology, Freiburg

1992-1997: Studies in Chemistry at the University of Freiburg

Specific Research Interests

- Signal Transduction
- Bacterial Protein Toxins
- Cytokine receptor signaling, JAK-STAT pathway
- Mechanisms of immune evasion used by Pasteurella multocida Toxin
- Osteoclastogenesis: Crosstalk between the skeletal and the immune system

Selected Publications

Kloos B, Chakraborty S, Lindner SG, Noack K, Harre U, Schett G, Krämer OH, Kubatzky KF: Pasteurella multocida Toxin induced osteoclastogenesis requires mTOR activation. **Cell Commun Signal 2015**; (accepted, September 2015)

Wiedenmann T, Ehrhardt S, Cerny D, Hildebrand D, Klein S, Heeg K, Kubatzky KF: Erythropoietin acts as an anti-inflammatory signal on murine mast cells. **Mol Immunol 2015**; 65(1): 68-76

Hildebrand D, Bode KA, Rieß D, Cerny D, Waldhuber A, Römmler F, Strack J, Korten S, Orth JH, Miethke T, Heeg K, Kubatzky KF: Granzyme A produces bioactive IL-1b through a non-apoptotic inflammasome-independent pathway. **Cell Rep 2014**; 6;9(3): 910-7

Hildebrand D, Sähr A, Wölfle SJ, Heeg K and Kubatzky KF: „Regulation of Toll-like receptor 4-mediated immune responses through Pasteurella multocida toxin-induced G protein signalling. **Cell Commun Signal 2012**; 1;10(1): 22

Reipschläger S, Kubatzky K, Taromi S, Burger M, Orth J, Aktories K and Schmidt G: Toxin-induced RhoA activity mediates CCL1-triggered STAT signalling. **J Biol Chem 2012**; 287(14): 11183-94

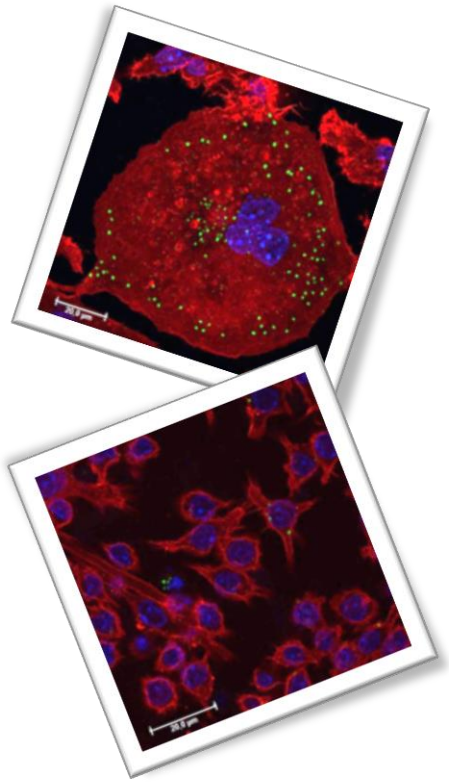
Hildebrand D, Heeg K and Kubatzky KF: Pasteurella multocida toxin stimulates B cell dependent osteoclast differentiation. **Infect Immun 2011**; 79(1)

Gündogdu MS, Liu H, Metzdorf D, Hildebrand D, Aigner M, Aktories K, Heeg K and Kubatzky KF: The haematopoietic GTPase RhoH modulates IL3 dependent proliferation through regulation of STAT activity and IL3 receptor expression. **Mol Cancer 2010**; 9(1): 225

Hildebrand D, Walker P, Dalpke AH, Heeg K and Kubatzky KF: Pasteurella multocida toxin induced Pim1 expression disrupts suppressor of cytokine signalling (SOCS)-1 activity. **Cell Microbiol 2010**; 12(12): 1732–1745

Preuss I, Hildebrand D, Orth JH, Aktories K and Kubatzky KF: Pasteurella multocida toxin is a potent activator of anti-apoptotic signalling pathways. **Cell Microbiol 2010**; 12(8): 1174-85

Orth JH, Aktories K and Kubatzky KF: Modulation of host cell gene expression through activation of STAT transcription factors by Pasteurella multocida toxin. **J Biol Chem 2007**; 282(5): 3050-7

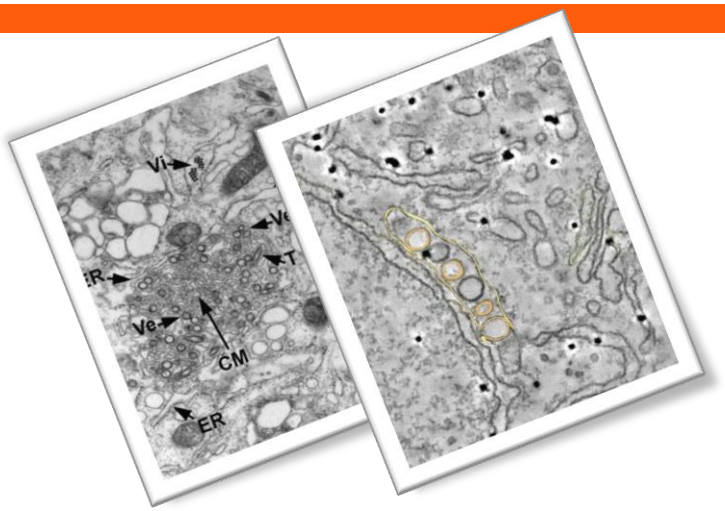


Molecular Virology

Fields of Interest

Teams in the department Molecular Virology work on several highly important human pathogens, namely hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV) as well as Dengue virus (DENV) and West Nile Virus (WNV). These viruses are leading causes for death worldwide with about 500 million people suffering from a chronic infection with either hepatitis B or C viruses and about 400 million new DENV infections occurring each year, especially in tropical countries.

As a department that focuses on molecular aspects of these infections, the following topics are studied: virus-host cell interaction, mechanism of host cell infection, virus assembly and involved host cell factors, RNA replication, viral and host cell factors suitable for antiviral therapy, RNA structures and their role for viral replication, mathematical modeling and simulation of virus replication, virus-induced host cell alterations, host cell stress response to virus infection, innate immune response and viral counter measures, antiviral therapy and therapy resistance. In order to cover these topics, we are using a broad and diverse array of methods and experimental approaches covering the fields of molecular biology, cell biology, biochemistry and immunology including live cell imaging and electron microscopy studies of infected cells.



The following teams belong to Molecular Virology:

-Prof. Dr. Ralf Bartenschlager (Head of the Molecular Virology)

-Prof. Dr. Stephan Urban

-PD Dr. Volker Lohmann

-Dr. Alessia Ruggieri

Prof. Dr. Ralf Bartenschlager

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Scientific Vita

2002-present: Full Professor and head of Molecular Virology, Department of Infectious Diseases, Heidelberg University, Germany; CHS Stiftungsprofessur "Molekulare Virologie"

2001: Full Professor for Molecular Biology, University of Mainz

1999: Habilitation, University of Mainz

1994-1998: Assistant, University of Mainz

1991-1993: PostDoc, Central Research Unit, Hoffmann-La Roche AG, Basel, Switzerland

1990: PhD in Molecular Biology, Heidelberg University

1981-1987: Studies in Biology, Heidelberg University

Specific Research Interests

- Virus - host cell interaction (esp. HCV and Dengue virus)
- Structural and functional aspects of viral RNA replication and assembly by using live cell imaging and electron microscopy techniques
- Viral and host targets for antiviral therapy
- Mathematical modeling of virus replication and spread as well as innate immune responses and viral countermeasures by using live cell imaging
- Viral persistence

Selected Publications

Poenisch M, Metz P, Blankenburg H, Ruggieri A, Lee JY, Rupp D, Rebhan I, Diederich K, Kaderali L, Domingues FS, Albrecht M, Lohmann V, Erfle H, Bartenschlager R: Identification of HNRNPK as regulator of hepatitis C virus particle production. **PLoS Pathog 2015**; 11(1): e1004573

Berger C, Romero-Brey I, Radujkovic D, Terreux R, Zayas M, Paul D, Harak C, Hoppe S, Gao M, Penin F, Lohmann V, Bartenschlager R: Daclatasvir-like inhibitors of NS5A block early biogenesis of hepatitis C virus-induced membranous replication factories, independent of RNA replication. **Gastroenterology 2014**; 147(5): 1094-105

Paul D, Madan V, Bartenschlager R: Hepatitis C virus RNA replication and assembly: living on the fat of the land. **Cell Host Microbe 2014**; 16(5): 569-79 Review

Romero-Brey I, Merz A, Chiramel A, Lee JY, Chlanda P, Haselman U, Santarella-Mellwig R, Habermann A, Hoppe S, Kallis S, Walther P, Antony C, Krijnse-Locker J, Bartenschlager R: Three-dimensional architecture and biogenesis of membrane structures associated with hepatitis C virus replication. **PLoS Pathog 2012**; 8(12): e1003056

Ruggieri A, Dazert E, Metz P, Hofmann S, Bergeest JP, Mazur J, Bankhead P, Hiet MS, Kallis S, Alvisi G, Samuel CE, Lohmann V, Kaderali L, Rohr K, Frese M, Stoecklin G, Bartenschlager R: Dynamic oscillation of translation and stress granule formation mark the cellular response to virus infection. **Cell Host Microbe 2012**; 12(1): 71-85

Reiss S, Rebhan I, Backes P, Romero-Brey I, Erfle H, Matula P, Kaderali L, Poenisch M, Blankenburg H, Hiet MS, Longerich T, Diehl S, Ramirez F, Balla T, Rohr K, Kaul A, Bühler S, Pepperkok R, Lengauer T, Albrecht M, Eils R, Schirmacher P, Lohmann V, Bartenschlager R: Recruitment and activation of a lipid kinase by hepatitis C virus NS5A is essential for integrity of the membranous replication compartment. **Cell Host Microbe 2011**; 9(1): 32-45

Welsch S, Miller S, Romero-Brey I, Merz A, Bleck CK, Walther P, Fuller SD, Antony C, Krijnse-Locker J, Bartenschlager R: Composition and three-dimensional architecture of the dengue virus replication and assembly sites. **Cell Host Microbe 2009**; 5(4): 365-75

Meylan E, Curran J, Hofmann K, Moradpour D, Binder M, Bartenschlager R, Tschopp J: Cardif is an adaptor protein in the RIG-I antiviral pathway and is targeted by hepatitis C virus. **Nature 2005;** 437(7062): 1167-72

Wakita T*, Pietschmann T*, Kato T, Date T, Miyamoto M, Zhao Z, Murthy K, Habermann A, Kräusslich HG, Mizokami M, Bartenschlager R*, Liang TJ. (* equal contribution): Production of infectious hepatitis C virus in tissue culture from a cloned viral genome**. Nat Med 2005;** 11(7): 791-6

Lohmann V, Körner F, Koch J, Herian U, Theilmann L, Bartenschlager R: Replication of subgenomic HCV RNAs in a hepatoma cell line. **Science 1999;** 285(5424): 110-3

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Scientific Vita

Since 2014: Full professor (W3) "Translational Virology" at the Medical Faculty ot the University of Heidelberg

2008-2014: Professorship (apl.) at the Faculty for Biosciences at the University of Heidelberg

2001-present: Research group leader at the Department of Infectious Diseases, Molecular Virology of the University Hospital Heidelberg

2000-2001: Stipendium at the ZMBH, Heidelberg University

2000: Habilitation at the faculty of Biosciences, Heidelberg University

1995-2000: PostDoc Center for Molecular Biology (ZMBH), Heidelberg University (Prof. Dr. H. Schaller)

1991-1995: PhD, Dept. of Virology (Prof. Dr. P. H. Hofschneider), Max-Planck-Institut für Biochemie, Martinsried

1991: Diploma in Biochemistry, University of Tübingen

Specific Research Interests

- Molecular mechanisms of Hepatitis B- and Hepatitis D Virus/host interactions with a focus on the early events of infection
- Identification of hepadnaviral receptors and structural analyses of virus receptor interactions
- Development of novel cell culture systems and animal models for HBV/HDV
- Clinical development of entry inhibitors (Myrcludex B) for HBV/HDV infection
- Development of hepatotropic drugs for the therapy of liver diseases

Selected Publications

Hoh A, Heeg M, Ni Y, Schuch A, Binder B, Hennecke N, Blum HE, Nassal M, Protzer U, Hofmann M, Urban S, Thimme R: HBV-infected HepG2hNTCP cells serve as a novel immunological tool to analyze the antiviral efficacy of CD8+ T cells in vitro. **J Virol 2015;** pii: JVI.00605-15

Slijepcevic D, Kaufman C, Wichers CG, Gilglioni EH, Lempp FA, Duijst S, de Waart DR, Oude Elferink RP, Mier W, Stieger B, Beuers U, Urban S, van de Graaf SF: Impaired uptake of conjugated bile acids and Hepatitis B Virus pres1-binding in Na+ -taurocholate cotransporting polypeptide knockout mice. **Hepatology 2015;** doi: 10.1002/hep.27694

Ni Y, Lempp FA, Mehrle S, Nkongolo S, Kaufman C, Fälth M, Stindt J, Königer C, Nassal M, Kubitz R and Urban S: Hepatitis B and D viruses exploit sodium taurocholate co-transporting polypeptide for species-specific entry into hepatocytes. **Gastroenterology 2014;** 146: 1070-1083

Urban S, Bartenschlager R, Kubitz R, Zoulim F: Strategies to inhibit entry of HBV and HDV into hepatocytes. **Gastroenterology 2014;** 7:48-64

Meier A, Mehrle S, Weiss TS, Mier W and Urban S: The myristoylated preS1-domain of the Hepatitis B Virus L-protein mediates specific binding to differentiated hepatocytes. **Hepatology 2012;** doi: 10.1002/hep.26181

Schulze A, Mills K, Weiss TS and Urban S: Hepatocyte polarization is essential for the productive entry of the hepatitis B virus**. Hepatology 2012;** 55(2): 373-383

Ni Y, Sonnabend J, Seitz S and Urban S: The pre-s2 domain of the hepatitis B virus is dispensable for infectivity but serves a spacer function for L-protein-connected virus assembly. **J Virol 2010;** 84: 3879-3888

Petersen J, Dandri M, Mier W, Lutgehetmann M, Volz T, von Weizsäcker F, Haberkorn U, Fischer L, Pollok JM, Erbes B, Seitz S and Urban S: Prevention of hepatitis B virus infection in vivo by entry inhibitors derived from the large envelope protein. **Nature Biotechnology 2008;** 26: 335-341

Seitz S*, Urban S*, Antoni C and Böttcher B: Cryo-electron microscopy of hepatitis B virions reveals variability in envelope capsid interactions. **EMBO J 2007;** 26: 4160-4167

Gripon P, Rumin S, Urban S, Le Seyec J, Glaise D, Cannie I, Guyomard C, Lucas J, Trepo C, Guguen-Guillouzo C: Infection of a human hepatoma cell line by hepatitis B virus. **PNAS 2002;** 99(24): 15655-15660

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Scientific Vita

2012: Habilitation, Heidelberg University

2002-present: Group Leader, Heidelberg University

1998-2002: PostDoc, Institute for Virology, University of Mainz

1993-1997: PhD, University of Mainz

1982-1993: Diploma Thesis, University of Mainz

1987-1992: Biology School, University of Mainz

Specific Research Interests

- Replication of hepatitis C virus and hepatitis A virus
- host cell factors of viral replication
- Lipid kinases and phosphatidylinositides
- Antiviral therapy and mode of action of inhibitors
- role of the innate immune system in virus control

Selected Publications

Grünvogel O, Esser-Nobis K, Reustle A, Schult P, Müller B, Metz P, Trippler M, Windisch MP, Frese M, Binder M, Fackler O, Bartenschlager R, Ruggieri A and Lohmann V: Dead box helicase 60-like (DDX60L) is an interferon stimulated gene restricting hepatitis C virus replication in cell culture. **J Virol 2015**; epub Aug 12. pii: JVI.01297-15

Esser-Nobis K, Harak C, Schult P, Kusov Y and Lohmann V: Novel perspectives for hepatitis A virus therapy revealed by comparative analysis of hepatitis C virus and hepatitis A virus RNA replication. **Hepatology 2015**; 62(2): 397-408

Harak C, Radujkovic D, Taveneau C, Reiss S, Klein R, Bressanelli S and Lohmann V: Mapping of functional domains of the lipid kinase phosphatidylinositol 4-kinase type III alpha involved in enzymatic activity and hepatitis C virus replication. **J Virol 2014**; 88(17): 9909-26

Esser-Nobis K, Romero-Brey I., Ganten T M, Gouttenoire J, Harak C, Klein R, Schemmer P, Binder M, Schnitzler P, Moradpour D, Bartenschlager R, Polyak SJ, Stremmel W, Penin F, Eisenbach C and Lohmann V: Analysis of hepatitis C virus resistance to silibinin in vitro and in vivo points to a novel mechanism involving nonstructural protein 4B. **Hepatology 2013**; 57:953-963.

Reiss, S., C. Harak, I. Romero-Brey, D. Radujkovic, R. Klein, A. Ruggieri, I. Rebhan, R. Bartenschlager, and Lohmann V: The lipid kinase phosphatidylinositol-4 kinase III alpha regulates the phosphorylation status of hepatitis C virus NS5A. **PLoS Pathog 2013**; 9:e1003359

Bartenschlager R, Lohmann V, Penin F: The molecular and structural basis of advanced antiviral therapy for hepatitis C virus infection. **Nat Rev Microbiol 2013**; 11(7): 482-96 Review

Lohmann V: Hepatitis C virus RNA replication. **Curr Top Microbiol Immunol 2013**; 369:167-98 Review

Reiss S, Rebhan I, Backes P, Romero-Brey I, Erfle H, Matula P, Kaderali L, Poenisch M, Blankenburg H, Hiet MS, Longerich T, Diehl S, Ramirez F, Balla T, Rohr K, Kaul A, Buhler S, Pepperkok R, Lengauer T, Albrecht M, Eils R, Schirmacher P, Lohmann V* and Bartenschlager R.*: Recruitment and activation of a lipid kinase by hepatitis C virus NS5A is essential for integrity of the membranous replication compartment. **Cell Host Microbe 2011**; 9: 32-45

Jo J, Aichele U, Kersting N, Klein R, Aichele P, Bisse E, Sewell AK, Blum HE, Bartenschlager R, Lohmann V* and Thimme R.*: Analysis of CD8+ T-cell-mediated inhibition of hepatitis C virus replication using a novel immunological model. **Gastroenterology 2009**; 136(4):1391-401

Lohmann V., Körner F, Koch JO, Herian U, Theilmann L and Bartenschlager R.: Replication of subgenomic hepatitis C virus RNAs in a hepatoma cell line. **Science 1999**; 285: 110-113

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Scientific Vita

2014-present: Independent group leader at the Department of Infectious Diseases, Heidelberg University

2008–2013: Postdoc at the Department of Infectious Diseases, Heidelberg University (Prof. R. Bartenschlager)

2004–2008: PostDoc at the Institute of Human Genetics, University of Saarland (Dr. J. Mayer)

1999–2003: PhD in Virology, École Normale Supérieure de Lyon, France

1998–1999: Diploma thesis, University of Lyon, France

1995–1998: Studies in Cellular and Molecular Biology Metz and Lyon, France

Specific Research Interests

- Dynamics of cellular stress and immune responses to HCV infection
- Identification of stress granule oscillation regulators
- Mathematical modeling of stress granule oscillations in response to RNA virus infection
- Modulation of the host cell translation by DENV infection
- Quantitative live-cell imaging

Selected Publications

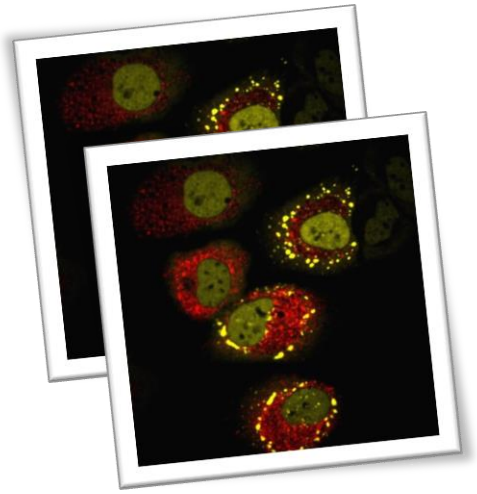
Hiet M-S, Bauhofer O, Zayas M, Roth H, Tanaka Y, Schirmacher P, Willemsen J, Grünvogel O, Bender S, Binder M, Lohmann V, Lotteau V, Ruggieri A†, Bartenschlager R†: Control of temporal activation of hepatitis C virus-induced interferon response by domain 2 of nonstructural protein 5A. **J Hepatol 2015**; pii: S0168-8278(15)00298-6

Ruggieri A, Bartenschlager R: Going full circle: Validation of P-body dispersion in hepatitis C virus-infected patients. **J Hepatol 2015**; 62(4):756-8

Ruggieri A, Dazert E, Metz P, Hofmann S, Bergeest JP, Mazur J, Bankhead P, Hiet MS, Kallis S, Alvisi G, Samuel CE, Lohmann V, Kaderali L, Rohr K, Frese M, Stoecklin G, Bartenschlager R: Dynamic oscillation of translation and stress granule formation mark the cellular response to virus infection. **Cell Host Microbe 2012**; 12(1): 71-85

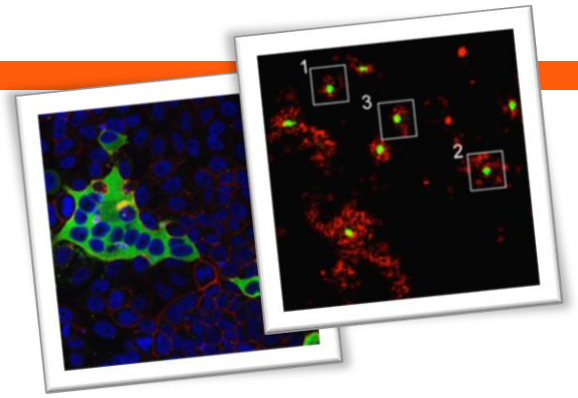
Bauhofer O, Ruggieri A, Schmid B, Schirmacher P, Bartenschlager R: Persistence of HCV in quiescent hepatic cells under conditions of an interferon-induced antiviral response. **Gastroenterology 2012**; 143(2): 429-438

Metz P, Dazert E, Ruggieri A, Mazur J, Kaderali L, Kaul A, Zeuge U, Trippler M, Lohmann V, Binder M, Frese M, Bartenschlager R: Identification of type I and type II interferon-induced effectors controlling hepatitis C virus replication. **Hepatology 2012**; 56(6):2082-93



Virology

Fields of Interest



Groups in Virology are interested in the molecular mechanisms leading to viral infection. The broad expertise of the various groups within the department allows us to dissect various steps in the viral life cycle, ranging from receptor binding to assembly and release, and to investigate pathogen-host interactions for a number of medically relevant viruses.

A major focus of our research is human immunodeficiency virus (HIV), the causative agent of AIDS (Kräusslich, Müller). In spite of more than 25 years of research, many questions concerning the biology of the virus remain unanswered; among these are surprisingly basic questions as 'Where does the virus enter the host cell?' or 'When and how is virus maturation initiated?' Our projects address the molecular and structural biology of the virus and its interaction with the host cell, including the evaluation of novel targets for antiviral therapy. We mainly focus on detailed analyses of virus morphogenesis and structure, as well as on the cell biology and dynamics of HIV entry, assembly and release. To address these topics, we combine traditional biochemical and virological approaches with advanced imaging techniques (live-cell imaging, novel fluorescent labeling strategies, various super-resolution fluorescence microscopy, (cryo)electron microscopy and -tomography, correlative microscopy, click chemistry) that we employ alone or together with strong collaborators. By this we aim at a quantitative and time resolved description of HIV-1 entry and morphogenesis, delineating the mechanistic role of viral and cellular factors (proteins and lipids) in these processes.

Other viral systems studied include parvoviruses, the enteropathogens norovirus and reovirus, bunyaviruses and influenza virus. We develop and use vectors based on adeno-associated virus for basic research and gene therapy approaches (Grimm) and exploit the CRISPR/Cas system for gene therapeutic and antiviral strategies (Grimm, Kräusslich). The Hansman group investigates the structural biology of the interaction of noroviruses, a major cause of infectious diarrhea, with cellular binding molecules. A further focus of interest is virus entry: the Lozach group is interested in entry pathways of bunyaviruses in the mammalian host and arthropod vector cells, whereas the Boulant group addresses the induction of innate immune response upon reovirus entry in human polarized intestinal epithelial cells and organoid systems. Finally, we are interested in influenza virus particle formation and entry, and in the role of host proteins and lipids in these processes (Kräusslich). Again, a combination of conventional virological approaches with a wide variety of specialized techniques (e.g. high throughput approaches, advanced microscopy techniques, x-ray crystallography and more) is employed to address the virological questions.

The following teams belong to the Virology:

-Prof. Dr. Hans-Georg Kräusslich (Head of the Virology)

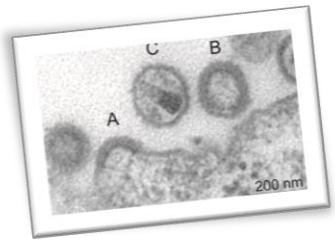
-apl. Prof. Dr. Barbara Müller

-Dr. Steeve Boulant

-Dr. Grant Hansman

-Dr. Dirk Grimm

-Dr. Pierre-Yves Lozach



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Scientific Vita

2004–present: Director Department of Infectious Diseases, Heidelberg University

2000–present: Full professor and head of virology, Heidelberg University

1995–1999: Full professor and head of department, Heinrich-Pette-Institute, Hamburg

1996–1999: Director, Heinrich-Pette-Institute, Hamburg

1993–1995: Head of junior department, German Cancer Research Centre, Heidelberg

1990: Habilitation, University of Heidelberg

1989–1993: Group leader, German Cancer Research Centre, Heidelberg

1986–1989: PostDoc, Dept. of Mol. Biology, State Univ. New York at Stony Brook

1985: MD in experimental virology (LMU Munich)

1977–1984: Medical School (LMU Munich)

Specific Research Interests

- Molecular virology
- cell biology of virus infection
- assembly, release and molecular architecture of HIV particles
- HIV Protease and antiviral resistance
- HIV-cell interactions
- Role of lipids in HIV replication
- Transmission and therapy of HIV infection

Selected Publications

Chlanda P, Schraidt O, Kummer S, Riches J, Oberwinkler H, Prinz S, Kräusslich HG***, Briggs JA***: Structural Analysis of the Roles of Influenza A Virus Membrane-Associated Proteins in Assembly and Morphology. **J Virol 2015**; 89:8957-66

Schneider J, Zahn J, Maglione M, Sigrist SJ, Marquard J, Chojnacki J, Kräusslich HG, Sahl SJ, Engelhardt J, Hell SW: Ultrafast, temporally stochastic STED

nanoscopy of millisecond dynamics. **Nat Methods 2015**; 12(9):827-30

Schur FKM, Hagen WJH, Rumlová M, Ruml T, Müller B, Kräusslich HG and Briggs JAG: The structure of the immature HIV-1 capsid in intact virus particles at 8.8 Å resolution. **Nature 2015**; 517:505-8

Peng K, Muranyi W, Glass B, Laketa V, Yant SR, Tsai L, Cihlar T, Müller B, Kräusslich HG: Quantitative microscopy of functional HIV post-entry complexes reveals association of replication with the viral capsid. **eLife 2014**; 10.7554/eLife.04114

Herold N, Anders-Ößwein M, Glass B, Eckhardt M, Müller B, Kräusslich HG: HIV-1 Entry in SupT1-R5, CEM-ss, and Primary CD4+ T Cells Occurs at the Plasma Membrane and Does Not Require Endocytosis. **J Virol 2014**; 88:13956-70

Engeland CE, Brown NP, Börner K, Schümann M, Krause E, Kaderali L, Müller GA, Kräusslich HG: Proteome analysis of the HIV-1 Gag interactome. **Virology 2014**; 460-461:194-206

Izquierdo-Useros N, Lorizate M, Puertas MC, Rodriguez-Plata MT, Zangger N, Erikson E, Pino M, Erkizia I, Glass B, Clotet B, Keppler OT, Telenti A, Kräusslich HG***, Martinez-Picado J***: Siglec-1 is a novel dendritic cell receptor that mediates HIV-1 trans-infection through recognition of viral membrane gangliosides. **PLoS Biol 2012**; 10(12):e1001448

Muranyi W, Malkusch S, Müller B, Heilemann M and Kräusslich HG: Super-resolution Microscopy Reveals Specific Recruitment of HIV-1 Envelope Proteins to Viral Assembly Sites dependent on the Envelope C-Terminal Tail. **PLoS Pathogens 2013**; 9(2):e1003198

Chojnacki J, Staudt T, Glass B, Bingen P, Engelhardt J, Anders M, Schneider J, Müller B, Hell SW, Kräusslich HG: Maturation Dependent HIV-1 Surface Protein Redistribution Revealed by Fluorescence Nanoscopy. **Science 2012**; 338:524-528

Carlson LA, de Marco A, Oberwinkler H, Habermann A, Briggs JA, Kräusslich HG, Grünewald K: Cryo electron tomography of native HIV-1 budding sites. **PLoS Pathogens 2010**; 6(11): e1001173

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Scientific Vita

2000-present: Group leader, Department of Infectious Diseases, Heidelberg

2004: Habilitation (Experimental Virology, Heidelberg University)

1995-2000: Postdoctoral fellow/research associate, Heinrich-Pette-Institute, Hamburg

1995: Postdoctoral fellow, German Cancer Research Center Heidelberg

1992-1995: Postdoctoral fellow, Fox Chase Cancer Center, Philadelphia, USA

1991-1992: Postdoctoral associate, MPI for Medical Research, Heidelberg

1991: Dr. rer. nat., Heidelberg University

1988-1991: PhD thesis (MPI for Med. Research Heidelberg, lab of R.S. Goody)

1987: Diploma (Heidelberg University)

1981-1986: Study of Biology (Technical University Darmstadt, Heidelberg University)

Specific Research Interests

- Biology of human immunodeficiency virus
- fluorescently labeled HIV-1 derivatives
- dynamics of HIV cell entry and HIV particle formation
- HIV assembly and maturation
- quantitative analysis of HIV replication steps

Selected Publications

Konvalinka J, Kräusslich HG, Müller B: Retroviral proteases and their roles in virion maturation. **Virology 2015**; doi: 10.1016/j.virol.2015.03.021

Mattei S, Flemming A, Anders-Össwein M, Kräusslich HG, Briggs JA, Müller B: RNA and Nucleocapsid Are Dispensable for Mature HIV-1 Capsid Assembly. **J Virol 2015**; 89:9739-47

Schimer J, Pavova M, Anders M, Pachl P, Sacha P, Cigler P, Weber J, Majer P, Rezacova P, Kräusslich HG, Müller B***, Konvlinka J***: Triggering HIV polyprotein processing inside virions by rapid photodegradation of a tight-binding photodestructable protease inhibitor. **Nature Communications 2015**; 6:6461

Hendrix J, Baumgärtel V, Schrimpf W, Ivanchenko S, Digman MA, Gratton E, Kräusslich HG, Müller B and Lamb DC: Live-cell observation of cytosolic HIV-1 assembly onset reveals RNA-interacting Gag oligomers. **J Cell Biol 2015**; 210:629-646

Schur FKM, Hagen WJH, Rumlová M, Ruml T, Müller B, Kräusslich HG and Briggs JAG: The structure of the immature HIV-1 capsid in intact virus particles at 8.8 Å resolution. **Nature 2015**; 517:505-8

Mattei S, Anders M, Konvalinka J, Kräusslich HG, Briggs JAG*** and Müller B***: Induced maturation of human immunodeficiency virus. **J Virol 2014**; 88:13722-31

Rahman SA, Koch P, Weichsel J, Godinez WJ, Schwarz U, Rohr K, Lamb DC, Kräusslich HG and Müller B: Investigating the role of F-actin in human immunodeficiency virus assembly by live-cell microscopy. **J Virol 2014**; 88:7904-14

Müller B and Heilemann M: Shedding new light on viruses: super-resolution microscopy for studying human immunodeficiency virus. **Trends in Microbiology 2013**; 21:522-33

Eckhardt M, Anders M, Muranyi W, Heilemann M, Krijnse-Locker J, Müller B: A SNAP-tagged derivative of HIV-1 -a versatile tool to study virus-cell interactions. **PLoS One 2011**; 6:e22007

Baumgärtel V, Ivanchenko S, Dupont A, Sergeev M, Wiseman PW, Kräusslich HG, Bräuchle C, Müller B***, Lamb DC***: Dynamics of HIV budding site interactions with an ESCRT component visualized in live cells. **Nat Cell Biol 2011**; 13: 469-474

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Scientific Vita

2012-present: Junior Group Leader CHS Foundation, University Hospital Heidelberg

2008-2012: Postdoctoral associate, Harvard Medical School Boston MA, USA

2006-2008: Marie curie Postdoctoral fellow, MRC Virology Unit Glasgow, UK

2005-2006: Postdoctoral associate, MRC Virology Unit Glasgow, UK

2004-2005: Bridging grant fellow, IBCP-CNRS Lyon, France

2001-2004: PhD in Molecular Biology and Biochemistry, IBCP-CNRS, France

2000-2001: DEA in Molecular Biology and Biochemistry (Master), Lyon, France

1998-2000: Bachelor degree in Molecular Biology and Biochemistry, Lyon, France

Specific Research Interests

- Characterization of the dynamic uptake, intracellular trafficking and endosomal rupture of non-enveloped viruses using live-cell confocal microscopy
- Evaluation of the forces exerted during viral entry
- Characterization of the kinetics and mechanism of clathrin structures
- Determining the anti-viral innate immune response in intestinal polarized epithelium cells
- Evaluation of the intracellular location and functional aspects of innate immunity sensor proteins (TLR and RLR) in polarized cells

Selected Publications

Odendall C, Dixit E, Stavru F, Bierne H, Franz KM, Durbin AF, Boulant S, Gehrke L, Cossart P, Kagan JC: Diverse intracellular pathogens activate type III interferon expression from peroxisomes. **Nat Immunol 2014**; 15(8):717-26

Blaising J, Lévy PL, Gondeau C, Phelip C, Varbanov M, Teissier E, Ruggiero F, Polyak SJ, Oberlies NH, Ivanovic T, Boulant S*, Pécheur EI*: Silibinin inhibits hepatitis C virus entry into hepatocytes by hindering clathrin-dependent trafficking. **Cellular Microbiology 2013**; 15(11):1866-82

Blaising J, Lévy PL, Polyak SJ, Stanifer M, Boulant S*, Pécheur EI*: Arbidol inhibits viral entry by interfering with clathrin-dependent trafficking. **Antiviral Res 2013**; 100(1):215-9

Boulant S*, Stanifer M, Kural C, Cureton DK, Massol R, Nibert ML, Kirchhausen T: Similar uptake but different trafficking and escape routes of reovirus virions and infectious subvirion particles imaged in polarized Madin-Darby canine kidney cells. **Mol Biol Cell 2013**; 24(8):1196-207

Cocucci E, Aguet F, Boulant S and Kirchhausen T: The first five seconds in the life of a clathrin coated pit. **Cell 2012**; 150(3):495-507

Kural C, Tacheva-Grigorova SK, Boulant S, Cocucci E, Baust T, Duarte D, Kirchhausen T: Dynamics of intracellular clathrin/AP1- and clathrin/AP3-containing carriers. **Cell Rep 2012**; 2(5):1111-9

Boulant S, Kural C, Zeeh JC and Kirchhausen T: Actin dynamics counteract membrane tension during clathrin-mediated endocytosis. **Nat Cell Biol 2011**; 13(9):1124-31

Dixit E, Boulant S, Zhang Y, Lee AS, Shum BOV, Hacohen N, Chen ZJ, Whelan SP, Fransen M, Nibert ML, Superti-Furga G, Kagan JC: Peroxisomes and mitochondria cooperate to induce antiviral innate immunity. **Cell 2011**; 141(4):668-81

Boulant S, Ivanovic T, Ehrlich M, Demidenko AA, Arnold MM, Kirchhausen T, Nibert ML: Recruitment of cellular clathrin factories and disruption of clathrin-depedent trafficking. **Traffic 2011**; 12(9):1179-95

Boulant S, Douglas M, Moody L, Budkowska A, Targett-Adams P and McLauchlan J: Hepatitis C virus core protein induces lipid droplet redistribution in a microtubule- and dynein-dependent manner. **Traffic 2008**; 9(8):1268-82

Dr. Grant Hansman

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Scientific Vita

2012-present: Group Leader, Heidelberg University and DKFZ, Germany

2005-2012: Senior Scientist, National Institute of Infectious Diseases, Japan

2001-2005: PhD, The University of Tokyo, Japan

1998-1999: Honors Degree, University of New South Wales, Australia

1993-1996: BSc, Macquarie University, Australia

Specific Research Interests

- Norovirus and other caliciviruses
- structural biology of viral proteins (X-ray crystallography and cryo-EM)
- drug discovery using X-ray crystallography
- antigenicity using virus-like particles
- molecular epidemiology of noroviruses
- zoonosis among caliciviruses
- human norovirus reverse genetics

Selected Publications

Hansman GS, Taylor DW, McLellan JS, Smith TJ, Georgiev I, Tame JRH, Park SY, Yamazaki M, Gondaira F, Miki M, Katayama K, Murata K, and Kwong PD: Structural basis for broad detection of genogroup II noroviruses by a monoclonal antibody that binds to a site occluded in the viral particle. **J Virol 2012**; 86: 3635-3646

Hansman GS, Shahzad-ul-Hussan S, McLellan JS, Chuang G, Georgiev I, Shimoike, T, Katayama K, Bewley, CA, and Kwong PD: Structural basis for norovirus inhibition and fucose mimicry by citrate. **J Virol 2012**; 86: 284-292

Hansman GS, Biertümpfel C, Georgiev I, McLellan JS, Chen L, Zhou T, Katayama K, Kwong PD: Crystal Structures of GII.10 and GII.12 Norovirus Protruding Domains in Complex with Histo-Blood Group Antigens Reveal Details for a Potential Site of Vulnerability. **J Virol 2011**; 85: 6687-6701

Ozawa K, Oka T, Takeda N Hansman GS: Norovirus infections in symptomatic and asymptomatic food handlers in Japan. **J Clin Microbiol 2007**; 45: 3996-4005

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Scientific Vita

2007-present: Group leader "Virus-Host Interactions", Heidelberg University Hospital

2006-2007: Research Associate, Stanford University, School of Medicine, CA, USA

2001-2006: Postdoctoral Fellow, Stanford University, School of Medicine, CA, USA

1999-2001: Postdoctoral Fellow, German Cancer Research Center, Heidelberg

1998: PhD (Biology) with Summa cum laude, University of Heidelberg

1994: Diploma (Biology), University of Kaiserslautern

1988-1994: Study of Biology (Universities of Kaiserslautern and Heidelberg)

Specific Research Interests

- Human gene therapy
- Viral and parasital infections (HIV, hepatitis viruses, Plasmodium)
- Adeno-associated viral (AAV) vectors
- Gene/genome engineering (CRISPR, TALENs)
- RNA interference (RNAi)
- Induced pluripotent stem cells (iPSC)
- Synthetic biology

Selected Publications

Mockenhaupt S, Grosse S, Rupp D, Bartenschlager R and Grimm D: Alleviation of off-target effects from vector-encoded shRNA via co-delivered RNA decoys. **PNAS 2015**; 112:E4007-16

Hentzschel F*, Hammerschmidt-Kamper C*, Börner K*, Heiss K*, Knapp B, Sattler JM, Kaderali L, Castoldi M, Bindman JG, Malato Y, Willenbring H, Mueller AK, and Grimm D: AAV8-mediated in vivo overexpression of miR-155 enhances the protective capacity of genetically-attenuated malarial parasites. **Mol Ther 2014**; 22:2130-41

Senís E*, Fatouros C*, Grosse S*, Wiedtke E, Niopek D, Mueller AK, Börner K and Grimm D: An adeno-associated viral (AAV) vector toolbox for CRISPR/Cas9-mediated genome engineering. **Biotechnol J 2014**; 9:1402-12

Schürmann N, Trabuco LG, Bender C, Russell RB and Grimm D: Molecular dissection of human Argonaute proteins using DNA family shuffling. **Nat Struct Mol Biol 2013**; 20:818-26

Börner K, Niopek D, Cotugno G, Kaldenbach M, Pankert T, Willemsen J, Zhang X, Schürmann N, Mockenhaupt S, Serva A, Hiet MS, Wiedtke E, Castoldi M, Starkuviene V, Erfle H, Gilbert DF, Bartenschlager R, Boutros M, Binder M, Streetz K, Kräusslich HG and Grimm D: Robust RNAi enhancement via human Argonaute-2 overexpression from plasmids, viral vectors and cell lines. **Nucleic Acids Res 2013**; 41:e199

Malato Y, Nagvi S, Schürmann N, Ng R, Wang B, Zape J, Kay M, Grimm D and Willenbring H: Fate-tracing of mature hepatocytes in mouse liver homeostasis and regeneration. **J Clin Invest 2011**; 121:4850-60

Grimm D, Wang L, Lee JS, Schürmann N, Gu S, Börner K, Storm TA and Kay MA: Argonaute proteins are key determinants of RNAi efficacy, toxicity, and persistence in the adult mouse liver. **J Clin Invest 2010**; 120:3106-19

Grimm D, Lee JS, Wang L, Desai T, Akache B, Storm TA and Kay MA. In vitro and in vivo gene therapy vector evolution via multispecies interbreeding and re-targeting of adeno-associated viruses. **J Virol 2008**; 82:5887-911

Grimm D, Streetz KS, Jopling CL, Storm TA, Pandey K, Davis CR, Marion P, Salazar F and Kay MA: Fatality in mice due to oversaturation of cellular microRNA/short hairpin RNA pathways. **Nature 2006**; 441:537-41

Grimm D, Zhou S, Nakai H, Thomas CE, Storm TA, Fuess S, Matsushita T, Allen J, Surosky R, Lochrie M, Meuse L, McClelland A, Colosi P and Kay MA: Pre-clinical in vivo evaluation of pseudotyped adeno-associated virus (AAV) vectors for liver gene therapy. **Blood 2003**; 102:2412-9

Dr. Pierre-Yves Lozach

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Scientific Vita

Since 2013: CellNetworks Group Leader, University Hospital Heidelberg

2012-2013: Assistant Professor, Pasteur Institute International Network, Laval, Canada

2010-2012: Senior Research Associate, ETH Zurich, Switzerland

2008-2010: Marie curie Post-doctoral fellow, ETH Zurich, Switzerland

2007-2008: Postdoctoral associate, ETH Zurich, Switzerland

2005-2007: Pediatric Dengue Vaccine Initiative postdoctoral fellow, Pasteur Institute, Paris, France

2001-2004: PhD in Fundamental Virology, Pasteur Institute, Paris, France

2000-2001: MSc in Fundamental Virology, Pasteur Institute, Paris, France

Specific Research Interests

- Arthropod-borne viruses (arboviruses) such as Rift Valley fever virus, Uukuniemi virus, and West Nile virus
- Cell biology of tick vector
- Transmission of arboviruses to humans
- Early virus-host cell interactions
- Dynamics of virus-receptor interactions
- Virus intracellular trafficking and entry
- Mechanisms of virus fusion
- Molecular determinants of arbovirus virulence and diseases

Selected Publications

Léger P and Lozach PY: Bunyaviruses: from transmission by arthropods to entry into mammalian-

host first-target cells. **Future Virology 2015**; 10(7):859-881

Boulant S*, Stanifer M, and Lozach PY*: Dynamics of virus-receptor interactions in virus binding, signaling, and endocytosis. **Viruses 2015**; 7(6):2794-2815

Meier R, Franceschini A, Horvath P, Tetard M, Mancini R, von Mering C, Helenius A and Lozach PY: Genome-wide siRNA screens reveal VAMP3 as a novel host factor required for Uukuniemi virus late penetration. **J Virol 2014**; 88(15):8565-78

Lozach PY*, Kühbacher A, Meier R, Mancini R, Bitto D, Bouloy M and Helenius A*: DC-SIGN as receptor for phleboviruses. **Cell Host Microbe 2011**; 10(1):75-88

Lozach PY, Huotari J, and Helenius A: Late-penetrating viruses. **Curr Opin Virol 2011**; 1:35-43

Lozach PY, Mancini R, Bitto D, Meier R, Oestereich L, Överby AK, Pettersson RF and Helenius A: Entry of bunyaviruses into mammalian cells. **Cell Host Microbe 2010**; 7(6):488-99

Mondotte JA, Lozach PY, Amara A and Gamarnik AV: Essential role of dengue virus envelope protein N glycosylation at asparagine-67 during viral propagation. **J Virol 2007**; 81(13):7136-48

Lozach PY, Burleigh L, Staropoli I, Navarro-Sanchez E, Harriague J, Virelizier JL, Rey FA, Despres P, Arenzana-Seisdedos F and Amara A: DC-SIGN mediated-enhancement of dengue virus infection is independent of DC-SIGN internalization signals. **J Biol Chem 2005**; 280(25):23698-708

Lozach PY, Amara A, Bartosch B, Virelizier JL, Arenzana-Seisdedos F, Cosset FL and Altmeyer R: C-type lectins L-SIGN and DC-SIGN capture and transmit infectious hepatitis C virus pseudotype particles. **J Biol Chem 2004**; 279(31):32035-45

Lozach PY, Lortat-Jacob H, de Lacroix de Lavalette A, Staropoli I, Foung S, Amara A, Houles C, Fieschi F, Schwartz O, Virelizier JL, Arenzana-Seisdedos F and Altmeyer R: DC-SIGN and L-SIGN are high affinity binding receptors for hepatitis C virus glycoprotein E2. **J Biol Chem 2003**; 278(22):20358-66

Integrative Virology

Fields of Interest

The central theme of our laboratories´ research is to integrate aspects of virology, host cell biology and immunology to understand basic principles of HIV-1 pathogenesis.

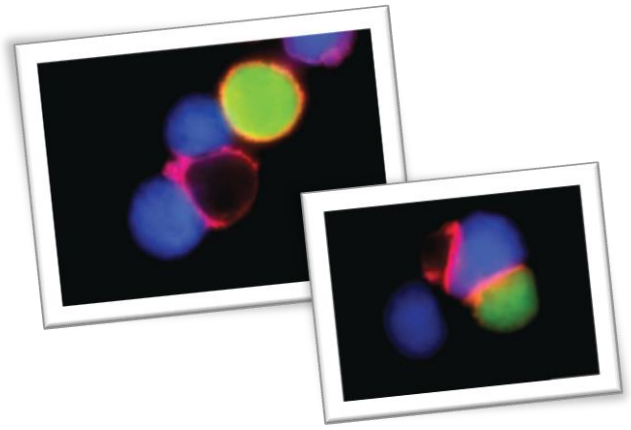
Part Fackler laboratory:

The studies of the Fackler laboratory focus currently on three specific aspects. First, we study the molecular mechanisms of action of the HIV-1 pathogenicity factor Nef. This involves assessing how Nef manipulates central host cell processes such as vesicular transport, signal transduction and cell motility. Second, we investigate how HIV-1 is recognized by the innate immune system of the host and the virus evades this response. These studies focus on intrinsic immunity factors such as CD317/BST-2/thetherin and SAMHD1 as well as the virally encoded antagonists Vpu and Vpx. Finally, we study the underlying mechanism that confer HIV-1 target cells resistance to infection. These analyses focus on resting $CD4+$ T lymphocytes that are refractory to productive infection with HIV-1 with the aim to define the barriers to infection but also the potential immunological consequences productive infection of these abundant target cells would have.

Methodology most commonly used in the lab includes flow cytometry, live cell and confocal microscopy, as well as approaches to study protein-protein interactions, all preferentially in primary HIV-1 target cells.

Part Lusic laboratory:

The studies of the Lusic laboratory focus on deciphering the cellular mechanisms used by the virus to either promote or repress viral gene expression. We investigate which parameters control integration of the viral genome and subsequent gene expression, with a strong focus on reactivation of viral gene expression after a silent phase of latency.



While an overall goal of our laboratory is to explore the specific contributions of nuclear topology and chromatin factors to HIV integration site selection and establishment of latency, we are specifically interested in determining the role of nuclear pore complex proteins in integration site selection. Moreover, we would like to focus on the interactions between nucleoporins with proteins that we previously found to contribute to proviral latency such as TRIM proteins.

Our methodology comprises the visualization of integrated HIV DNA in host cells by using a combination of 3D Immuno DNA FISH and Chromatin Immunoprecipitation technology.

The following teams belong to the Integrative Virology:

-Prof. Dr. Oliver T. Fackler (Head of the Integrative Virology)

-Dr. Marina Lusic

Prof. Dr. Oliver T. Fackler

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Scientific Vita

2013-present: Head of section Integrative Virology, Department of Infectious Diseases, Virology, Heidelberg University

2007-present: W3 professor at the Department of Infectious Diseases, Virology, Heidelberg University

2003: Habilitation in experimental virology, Heidelberg University

2000-2007: Group leader, Department of Virology, Heidelberg University

1997-2000: Postdoctoral fellow, University of California at San Francisco

1994-1997: PhD in molecular virology (Homburg/Saar)

1993-1994: Diploma thesis in molecular virology (Homburg/Saar)

1989-1993: Studies in biology (Saarbrücken)

Specific Research Interests

- Immuno- and cell biology of HIV infection
- innate and instrinsic immunity against HIV-1 and viral evasion thereof
- HIV accessory genes

Selected Publications

Fackler OT*, Murooka TT, Imle A and Mempel TR*: Adding new dimensions: Towards an integrative understanding of HIV-1 spread. **Nat Rev Microbiol 2014**; 12:563-574

Kutscheidt S+, Zhu R+, Antoku S+, Luxton GGW, Stagljar I, Fackler OT* and Gundersen G*: FHOD1 interaction with nesprin-2G mediates TAN line formation and nuclear movement. **Nat Cell Biol 2014**; 16: 708-715

Baldauf HM+, Pan X+, Erikson E, Schmidt S, Daddacha W, Burggraf M, Schenkova K, Ambiel I, Wabnitz G, Gramberg T, Panitz S, Flory E, Landau NR, Sertel S, Rutsch F, Lasitschka F, Kim B, König R, Fackler OT* and Keppler OT*: The deoxynucleoside triphosphate triphosphohydrolase SAMHD1 restricts HIV-1 infection in resting CD4+ T cells. **Nat Med 2012**; 18: 1682-1687

Stolp B, Imle A, Coelho FM, Hons M, Mendiz RG, Lyck R, Stein JV and Fackler OT: HIV-1 Nef Interferes With T Lymphocyte Circulation Through Confined Environments in vivo. **PNAS 2012**; 109: 18541–18546

Pan X, Rudolph JM, Abraham L, Habermann A, Haller C, Krijnse-Locker J and Fackler OT: HIV-1 Nef Compensates Disorganization of the Immunological Synapse by Assembly of an Intracellular Lck Signalosome. **Blood 2012**; 119: 786-797

Stastna J, Pan XY, Wang H, Kollmannsperger A, Kutscheid S, Lohmann V, Grosse R and Fackler OT: Differing and isoform specific roles for the formin DIAPH3 in plasma membrane blebbing and filopodia formation. **Cell Research 2012**; 22: 728–745

Stolp B, Raichman-Fried M, Abraham L, Pan X, Giese SI, Hannemann S, Goulimari P, Raz E, Grosse R and Fackler OT: HIV-1 Nef interferes with host cell motility by deregulation of cofilin. **Cell Host Microbe 2009**; 6:174-186

Goffinet C, Allespach A, Homann S, Tervo HM, Habermann A, Rup, D, Oberbremer L, Kern C, Tibroni N, Welsch S, Krijnse-Locker J, Banting G, Kräusslich HG, Fackler OT and Keppler OT: HIV-1 Antagonism of CD317 is Species-Specific and Involves Vpu-Mediated Proteasomal Degradation of the Restriction Factor. **Cell Host Microbe 2009**; 5: 285-297

Fackler OT*, Alcover A and Schwartz O*: Modulation of the Immunological Synapse: A key to HIV-1 pathogenesis? **Nat Rev Immunol 2007**; 7: 310-317

Fackler OT, Luo W, Geyer M, Alberts AS and Peterlin BM: Activation of Vav by Nef induces cytoskeletal rearrangements and downstream effector functions. **Mol Cell 1999**; 3: 729-739

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Scientific Vita

2014-present: Group leader, Department of Infectious Diseases, Heidelberg

2009-2014: Extended faculty member/project leader at San Raffaele Scientific Institute, Milan and ICGEB, Trieste, Italy

2004-2009: PostDoc, ICGEB, Trieste, Italy

2003: PhD degree in Molecular Biology and Biochemistry, Faculty of Biological Sciences, University of Belgrade

1999-2004: Long term ICGEB Fellowship, Molecular Medicine Laboratory, International Centre for Genetic Engineering and Biotechnology (ICGEB), Trieste, Italy

1998: Magister of Science, Biochemistry and Molecular Biology, University of Belgrade

Specific Research Interests

- Nuclear organization and chromatin changes in viral infection
- HIV-1 transcriptional regulation and latency
- Trim family proteins and control of HIV-1 integration and transcription

Selected Publications

Marini B, Kertesz-Farkas A, Lucic B, Hashim A, Lisek K, Manganaro L, Pongor S, Luzzati R, Mavilio F, Giacca M and Lusic M: Nuclear architecture dictates HIV-1 integration site selection. **Nature 2015**; 521 (7551): 227-31, Epub 2015 Mar 2

Lusic M and Giacca M: Ground Control to Major Tom: "Prepare for HIV Landing". **Cell Host Microbe 2014**;Vol 16(5): 557–559

Lusic M and Giacca M: Regulation of HIV-1 latency by chromatin structure and nuclear architecture. **J Mol Biol 2014**; 427(3):688-94 Review

Quy VC, Carnevale V, Manganaro L, Lusic M, Rossetti G, Leone V, Fenollar-Ferrer C, Raugei S, Del Sal G, Giacca M, Carloni P: HIV-1 integrase binding to its cellular partners: a perspective from computational biology. **Curr Pharm Des 2014**; 20(21): 3412-21

Lusic M, Marini B, Ali H, Lucic B, Luzzati R and Giacca M: Proximity to PML Nuclear Bodies negatively regulates HIV-1 gene expression in CD4+ T cells. **Cell Host Microbe 2013**; 13: 665-677. Research highlight in Science Vol 341 (2013) p:11 and in Cell Host Microbe Vol 13:625-626

Della Chiara G, Crotti A, Liboi E, Giacca M, Poli G and Lusic M: Negative Regulation of HIV-1 Transcription by a Heterodimeric NF-κB1/p50 and C-Terminally Truncated STAT5 Complex. **J Mol Biol 2011**; 410 (5): 933-943

Allouch A, Di Primio C, Alpi E, Lusic M, Arosio D, Giacca M and Cereseto A: KAP-1 inhibits HIV-1 integration. **Cell Host Microbe 2011**; 9 (6): 484-95

Manganaro L, Lusic M*, Gutierrez MI, Cereseto A, Del Sal G and Giacca M*: Concerted action of cellular JNK and Pin-1 restricts HIV-1 genome integration to activated $CD4^+$ T lymphocytes. **Nat Medicine 2010**; 16 (3): 329-323

Dieudonné M, Maiuri P, Biancotto C, Knezevich A, Kula A, Lusic M, and Marcello A: Transcriptional competence of the integrated HIV-1 provirus at the nuclear periphery. **EMBO J 2009**; 28 (15):2231-2243

Perkins KJ, Lusic M, Mitar I, Giacca M and Proudfoot NJ: Transcription dependent gene looping of the HIV-1 provirus is dictated by recognition of pre-mRNA processing signals. **Molecular Cell 2008**; 29 (1) 56-68

Parasitology

Fields of Interest

Malaria has remained one of the most important infectious diseases worldwide, causing an estimated 200 Million clinical cases and killing 600,000 people *every* year. Hopes of malaria control have been thwarted by widespread drug resistances. Malaria is caused by protozoan parasites of the genus Plasmodium, of which Plasmodium falciparum is the most virulent form. Infection starts with the bite of an infected Anopheles mosquito that transmits *infective* stages termed sporozoites into the human body. Sporozoites are carried with the blood flow to the *liver* where they *invade* hepatocytes. After completing their development within the *liver,* the parasite is released and now *invades* erythrocytes. Intra-erythrocytic *dev*elopment of the parasite is responsible for the clinical manifestation of the disease, including intermittent *fever,* shaking chills, organ dysfunction and the syndromes associated with cerebral and maternal malaria. *Severe* complications result from the ability of infected erythrocytes to adhere to the endothelial lining of venular capillaries and to sequester in the deep vascular bed.

The following teams belong to the Parasitology Unit:

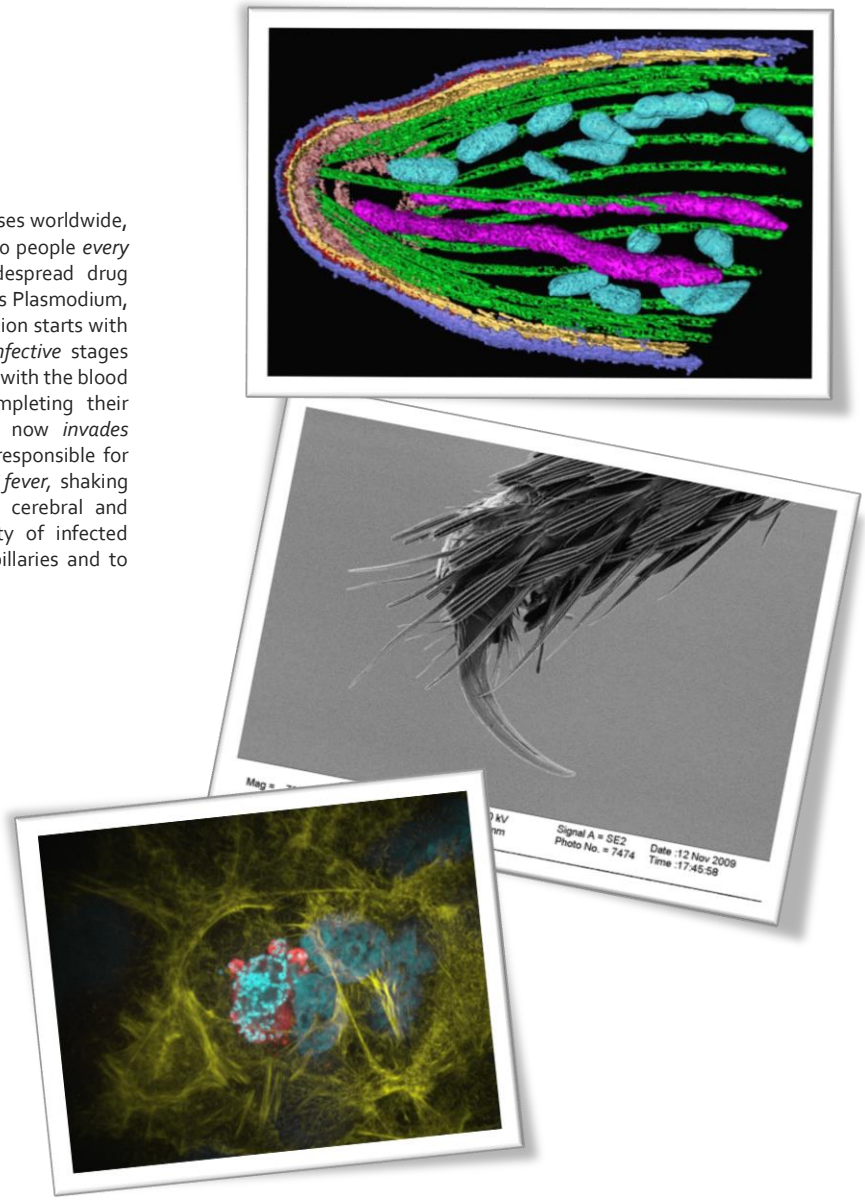
-Prof. Dr. Michael Lanzer (Head of the Parasitology Unit)

-apl. Prof. Dr. Marcel Deponte

-Dr. Christian Epp (until 31 December 2015)

-Prof. Dr. Friedrich Frischknecht

-Dr. Ann-Kristin Mueller



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Scientific Vita

2000: Chair of Parasitology offered by the Seattle Biomedical Institute, USA (declined)

1999: Full Professor & Department Chair of Parasitology, Heidelberg University

1996: Habilitation in Microbiology, University of Würzburg

1994-1998: Junior Group Leader, Research Center for Infectious Diseases, University of Würzburg

1988-1993: PostDoc, Sloan-Kettering Inst., New York

1985-1988: Graduate Student, Center for Molecular Biology, Heidelberg University

1984-1985: Undergraduate Student, Hoffman LaRoche AG, Basel

Specific Research Interests

- Molecular Parasitology
- drug resistance mechanisms of the malarial parasite
- antigenic variation, cytoadherence, protein trafficking in *P. falciparum*
- membrane transport processes

Selected Publications

Rieger H, Yoshikawa HY, Quadt K, Nielsen MA, Sanchez CP, Salanti A, Tanaka M and Lanzer M: Cytoadhesion of Plasmodium falciparum-infected erythrocytes to chondroitin-4-sulfate is cooperative and shear enhanced. **Blood 2015**; 125: 383-391

Sanchez CP, Liu CH, Mayer S, Nurhasanah A, Cyrklaff M, Mu J, Ferdig MT, Stein WD and Lanzer M: A HECT ubiquitin-protein ligase as a novel candidate gene for altered quinine and quinidine responses in Plasmodium falciparum. **PLoS Genet 2014**; 10: e1004382

Summers RL, Dave A, Dolstra TJ, Bellanca S, Marchetti RV, Nash MN, Richards SN, Goh V, Schenk RL, Stein WD, Kirk K, Sanchez CP, Lanzer M and Martin RE: Diverse mutational pathways converge on saturable chloroquine transport via the malaria parasite's chloroquine resistance transporter. **PNAS 2014**; 111: E1759-1767

Cyrklaff M, Sanchez CP, Kilian N, Bisseye C, Simpore J, Frischknecht F and Lanzer M: Hemoglobins S and C interfere with actin remodeling in Plasmodium falciparum-infected erythrocytes. **Science 2011**; 334: 1283-1286

Rohrbach P, Sanchez CP, Hayton K, Friedrich O, Patel J, Sidhu AB, Ferdig MT, Fidock DA and Lanzer M: Genetic linkage of pfmdr1 with food vacuolar solute import in Plasmodium falciparum. **Embo J 2006**; 25: 3000-3011

Przyborski JM, Miller SK, Pfahler JM, Henrich PP, Rohrbach P, Crabb BS and Lanzer M: Trafficking of STEVOR to the Maurer's clefts in Plasmodium falciparum-infected erythrocytes. **Embo J 2005**; 24: 2306-2317

Sanchez CP, Stein W and Lanzer M: Trans stimulation provides evidence for a drug efflux carrier as the mechanism of chloroquine resistance in Plasmodium falciparum. **Biochemistry 2003**; 42: 9383-9394

del Portillo HA, Fernandez-Becerra C, Bowman S, Oliver K, Preuss M, Sanchez CP, Schneider NK, Villalobos JM., Rajandream MA, Harris D, Pereira da Silva LH, Barrell B and Lanzer M: A superfamily of variant genes encoded in the subtelomeric region of Plasmodium vivax. **Nature 2001**; 410: 839-842

Scherf A, Hernandez-Rivas R, Buffet P, Bottius E, Benatar C, Pouvelle B, Gysin J and Lanzer M: Antigenic variation in malaria: in situ switching, relaxed and mutually exclusive transcription of var genes during intra-erythrocytic development in Plasmodium falciparum. **Embo J 1998**; 17: 5418-5426

Lanzer M, de Bruin D and Ravetch JV: Transcriptional differences in polymorphic and conserved domains of a complete cloned P. falciparum chromosome. **Nature 1993**; 361: 654-657

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Scientific Vita

2014-present: Heisenberg scholarship

2014: Appointment as apl. Prof.

2011: Habilitation in Biochemistry, Heidelberg University

2010-present: Independent group leader, Dept. of Infectious Diseases, Parasitology, Heidelberg University Hospital

2006-2010: Junior group leader, Institute of Physiological Chemistry, L.M.-University Munich

2005-2006: Postdoc, J.L.-University Gießen & WEHI Melbourne

2002-2005: PhD student, Biochemistry, Interdisciplinary Research Center, J.L.-University Gießen

1997-2002: Diploma student, Biochemistry, E.K.-University Tübingen

Specific Research Interests

- molecular parasitology & enzymology
- mitochondrial protein import in parasitic protists (*Plasmodium* and *Leishmania*)
- redox catalysis and inhibitors
- glutathione-dependent enzymes
- comparative molecular evolution

Selected Publications

Staudacher V*, Djuika CF*, Koduka J*, Schlossarek S*, Kopp J, Büchler M, Lanzer M and Deponte M: Plasmodium falciparum antioxidant protein reveals a novel mechanism for balancing turnover and inactivation of peroxiredoxins. **Free Radic Biol Med 2015**; 85:228-36

Begas P, Staudacher V and Deponte M: Systematic re-evaluation of the bis(2-hydroxyethyl)disulfide (HEDS) assay reveals an alternative mechanism and activity of glutaredoxins. **Chem Science 2015**; 6:3788-96

Djuika CF, Huerta-Cepas J, Przyborski JM, Deil S, Sanchez CP, Doerks T, Bork P, Lanzer M and Deponte M: Prokaryotic ancestry and gene fusion of a dual localized peroxiredoxin in malaria parasites. **Microbial Cell 2015**; 2:5-13

Eckers E, Petrungaro C, Groß D, Riemer J, Hell K and Deponte M: Divergent molecular evolution of the mitochondrial sulfhydryl:cytochrome c oxidoreductase Erv in opisthokonts and parasitic protists. **J Biol Chem 2013**; 288:2676-88

Ehrhardt K, Davioud-Charvet E, Ke H, Vaidya A, Lanzer M and Deponte M: The antimalarial activities of methylene blue and the 1,4-naphthoquinone 3-[4-(trifluoromethyl)benzyl]-menadione are not due to inhibition of the mitochondrial electron transport chain. **Antimicrob Agents Chemother 2013**; 57:2114-20

Djuika C, Fiedler S, Schnölzer M, Sanchez C, Lanzer M and Deponte M: Plasmodium falciparum antioxidant protein as a model enzyme for a special class of glutaredoxin/glutathione-dependent peroxiredoxins. **Biochim Biophys Acta 2013**; 1830:4073-90

Deponte M: Glutathione catalysis and the reaction mechanisms of glutathione-dependent enzymes. **Biochim Biophys Acta 2013**; 1830:3217-66

Eckers E, Cyrklaff M, Simpson L and Deponte M: Mitochondrial protein import pathways are functionally conserved among eukaryotes despite compositional diversity of the import machineries. **Biol Chem 2012**; 393:513-24

Urscher M, Alisch R and Deponte M: The glyoxalase system of malaria parasites - Implications for cell biology and general glyoxalase research. **Semin Cell Dev Biol 2011**; 22:262-70

Harner M, Neupert W and Deponte M: Lateral release of proteins from the TOM complex into the outer membrane of mitochondria. **EMBO J 2011**: 30:3232-41

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Scientific Vita

2005-present: Group Leader, Center of Infectious Diseases, Parasitology, Heidelberg University Hospital

2001-2005: Postdoc, Institut Pasteur, Paris, France

2000: PhD, FU Berlin (summa cum laude)

1996-2000: PhD thesis, EMBL, Heidelberg

1995-1996: Research student, Lab of Molecular Biology, Cambridge, UK

1990-1996: Studies of Biochemistry (FU Berlin)

Specific Research Interests

- cell biology and biophysics of pathogen infection
- malaria cell biology
- live cell imaging
- cell motility

Selected Publications

Douglas RG, Amino R, Sinnis P, Frischknecht F: Active migration and passive transport of malaria parasites. **Trends Parasitol 2015**; 31(8):357-62

Hegge S, Uhrig K, Streichfuss M, Kynast-Wolf G, Matuschewski K, Spatz JP and Frischknecht F: Direct manipuation of malaria parasites with optical tweezers reveals distinct functions of Plasmodium surface proteins. **ACS Nano 2012**; 6. 4648-4662

Kudryashev M, Münter S, Lemgruber L, Montagna G, Matuschewski K, Stahlberg H, Meissner M, Cyrklaff M, Frischknecht F: Structural basis for chirality and directional motility of Plasmodium sporozoites. **Cellular Microbiology 2012**; 14, 1757-1768

Perschmann N, Hellmann JK, Frischknecht F#, and Spatz JP#: Induction of malaria parasite migration by synthetically tunable microenvironments. **Nano Letters 2011**; 11, 4468-4474. Erratum in: Nano Lett 2012; 12(8):4414

Hellmann JK, Münter S, Kudryashev M, Schulz S, Heiss K, Müller AK, Matuschewski K, Spatz JP, Schwarz US and Frischknecht F: Environmental constraints guide migration of malaria parasites during transmission. **PLoS Pathogens 2011**; 7, e1002080

Hegge S, Münter S, Steinbüchel M, Heiss K, Engel U, Matuschewski K and Frischknecht F: Multistep adhesion of Plasmodium sporozoites. **FASEB Journal 2010**; 24, 2222-2234

Münter S, Sabass B, Selhuber-Unkel C, Kudryashev M, Hegge S, Spatz JP, Engel U, Matuschewski K, Schwarz US# and Frischknecht F#: Plasmodium sporozoite motility is modulated by the turnover of discrete adhesion sites. **Cell Host Microbe 2009**; 6: 551-562

Kudryashev M, Cyrklaff M, Baumeister W, Simon MM, Wallich R# and Frischknecht F#: Comparative cryo-electron tomography of pathogenic Borrelia species. **Molecular Microbiology 2009**; 71, 1415-1434

Cyrklaff M#, Kudryashev M, Leis A, Leonard K, Baumeister W, Ménard R, Meissner M and Frischknecht F#: Cryoelectron tomography reveals periodic luminal material in subpellicular microtubules from apicomplexan parasites. **Journal of Experimental Medicine 2007**; 204, 1281-1287

Amino R#, Thiberge S, Martin B, Celli S, Shorte SL, Frischknecht F# and Ménard R#: Quantitative imaging of malaria parasite transmission to the mammalian host. **Nature Medicine 2006**; 12, 220-224

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Scientific Vita

2015: Awarded a DZIF Maternity Leave stipend

2012: Awarded the Minerva-Arches prize

2011: Founder and Mentor of MalVa GmbH

2009-present: Independent Group Leader, Heidelberg University Hospital

2007-2008: Junior Group Leader, Research Center for Infectious Diseases, University of Würzburg

2007: EMBO long-term research fellow at LSHTM, London with Prof. E. Riley

2006: Awarded the 2006 prize for basic medical research by the GlaxoSmithKline foundation

2006: Awarded the Karl Freudenberg prize by the Heidelberger Akademie der Wissenschaften

2004-2006: Postdoctoral Fellow with Prof. K. Matuschweski

2001-2004: Graduate Student, Ruprecht-Karls University Heidelberg with Prof. K. Matuschewski (Parasitology)

2000-2001: Diploma thesis with Prof. E. Bremer, Philipps University Marburg (Microbiology)

1996-2000: Undergraduate Student, Philipps University Marburg

Specific Research Interests

- Molecular Parasitology
- Vaccinology
- protective immunity
- murine malaria
- T-cell immunology
- host-pathogen interactions

Selected Publications

Lewis MD, Behrends J, Sa e Cunha C, Mendes A, Lasitschka F, Sattler JM, Heiss K, Kooij T, Prudendcio M, Bringmann G, Frischknecht F, Mueller AK: Chemical attenuation of Plasmodium in the liver modulates severe malaria disease progression. **J Immunol 2015**; 1400863 [Epub ahead of print]

Pfeil J, Heine JF, Mueller AK: Addition of histamine to subcutaneously injected Plasmodium berghei sporozoites increases the parasite liver load and could facilitate whole-parasite vaccination. **Malar J 2015**; 28; 14(1): 36

Hentzschel F, Hammerschmidt-Kamper C, Börner K, Heiss K, Knapp B, Sattler JM, Kaderali L, Castoldi M, Bindman JG, Malato Y, Willenbring H, Mueller AK*, Grimm D*: AAV8-mediated in vivo overexpression of miR-155 improved vaccination against experimental malaria. **Mol Ther 2014**; 10.1038/mt.2014.172

Lewis MD, Pfeil J, Heiss K, Mueller AK: CD8+ T cells mediate robust stage-specific immunity to P.berghei under chemoprophylaxis and this protective environment is not downregulated by blood-stage infection. **PLoS One 2014**; 9(2): e88117. 10.1371/journal.pone.0088117. eCollection 2014

Lödige M, Lewis MD, Paulsen E, Esch H., Pradel G, Lehmann L, Brun R, Bringmann G, Mueller AK: An antiplasmodial hybrid agent with a dual mode of action: Innovative advancement of aproved drugs. **Int J Med Microbiol 2013**; 1438-4221(13)00101-X. 10.1016/j.ijmm.2013.07.005

Mueller AK, Deckert M, Heiss K, Goetz K, Matuschewski K, Schluter D: Genetically Attenuated Plasmodium berghei Liver Stages Persist and Elicit Sterile Protection Primarily via CD8 T Cells. **Am J Pathol 2007**; 171(1): 107-115

Jobe O, Lumsden J, Mueller AK, Williams J, Silva-Rivera H, Kappe S.H, Schwenk R.J, Matuschewski K, Krzych U: Genetically Attenuated Plasmodium berghei Liver Stages Induce Sterile Protracted Protection that Is Mediated by Major Histocompatibility Complex Class I-Dependent Interferon-gamma-Producing CD8+ T Cells. **J Infect Dis 2007**; 96(4): 599-607

Schuler H, Mueller AK, Matuschewski K: A Plasmodium Actin-depolymerizing Factor That Binds Exclusively to Actin Monomers. **Mol Biol Cell 2005**; 16(9): 4013-23

Mueller AK, Camargo N, Kaiser K, Andorfer C, Frevert U, Matuschewski K, Kappe SH: Plasmodium liver stage developmental arrest by depletion of a protein at the parasite-host interface. **PNAS 2005**; 22;102(8): 3022-7

Mueller AK, Labaied M, Kappe SH, Matuschewski K: Genetically modified Plasmodium parasites as a protective experimental malaria vaccine. **Nature 2005**; 13; 433(7022): 164-7

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Scientific Vita

1990-present: Professor for Microbiology, University of Heidelberg

1990-1990: Associate Professor, The Rockefeller University, New York USA

1983-1990: Assistant Professor, The Rockefeller University, New York USA

1981-1983: Postdoctoral Fellow, Stanford University Medical Center, California, USA

1978-1981: Postdoctoral Fellow, Imperial College, London, UK

1979: PhD (Zoology) University of London, UK

1975-1978: PhD student, National institute for Medical research, Mill Hill, London, UK

1972-1975: Bachelor of natural Sciences, major Biochemistry, University of Cambridge, UK

Specific Research Interests

- Regulation of mRNA decay and translation in trypanosomes

Selected Publications

Clayton C: Networks of gene expression control in trypanosomes. **Mol Biochem Parasitol 2014**; 195, 96-106 Review

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