



DEPARTMENT OF INFECTIOUS DISEASES, HEIDELBERG UNIVERSITY

Department of Infectious Diseases

Major Infectious Diseases

Research Groups of the Department of Infectious Diseases

Infectious Diseases - A Brief Description

Although infectious diseases have been known for thousands of years, the understanding of their source emerged only in the past century. Thus, the study of infectious diseases at the molecular and cellular level is a rather new research area, whose origin as an independent scientific discipline can be traced back to the discovery of pathogenic microorganisms in the 19th century.

Today it is common knowledge that infectious diseases are caused by bacteria, viruses, fungi and parasites. Although a lot has been learned about human pathogens in the past decades, infectious diseases continue to be a major threat for human health. Not only well known diseases like malaria, AIDS or chronic hepatitis, but also gastrointestinal or respiratory infections result in millions of deaths each year. Rapid evolution of pathogens and a changing environment result in rising threats from multiresistant bacteria or the emergence and spread of pathogens including novel strains of influenza virus, MERS or Dengue virus. Furthermore, advances in medicine have led to an increased number of immunocompromised people who are particularly susceptible to infectious diseases.

Apart from their enormous medical importance, microbes are also 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 initially for DNA viruses.

Current infectious disease research is a highly interdisciplinary topic at the interface between medicine and molecular, cell and structural biology. The 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

Main research topics of the Department include HIV/Aids, malaria, viral hepatitis and the interaction between pathogens and their host (immunology of infection, pathogen spread) (<https://www.klinikum.uni-heidelberg.de/UEberblick.1208.o.html>).

Researchers from all units are integrated within the new Center for Integrative Infectious Disease Research, where replication and spread of pathogens is studied in systems of increasing complexity, from molecular detail to interaction with the host immune response in 3D culture systems or animal models. Interactions will be

further strengthened upon opening of the new CIID building in 2017, offering state of the art equipment, in particular for various types of advanced imaging.

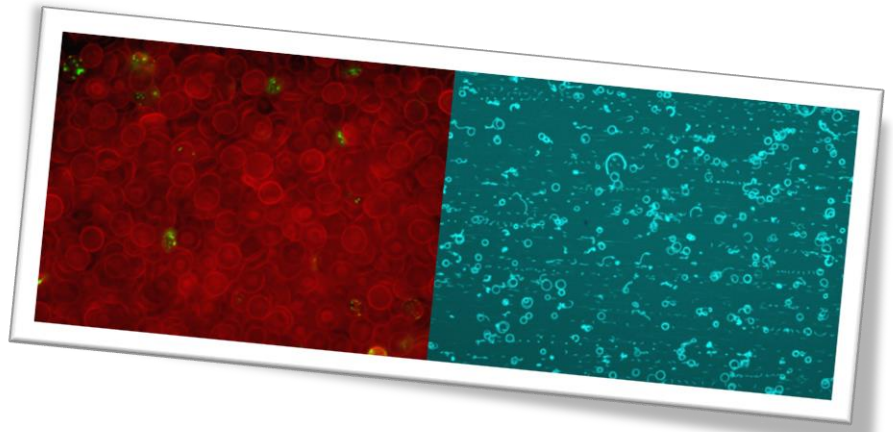
Beyond that, all research groups of the department are connected within local and international research consortia and networks, some of which are coordinated by members of the department. This comprises the Cluster of Excellence "CellNetworks" (<http://www.cellnetworks.uni-hd.de/>) as well as DFG collaborative research centers SFB1129 (<http://www.sfb1129.de/>), SFB-TR179 (web tba) and SFB-TR83 (<http://www.trr83.de/>) and the DFG priority program 1923 (web tba).

We cooperate with numerous institutions from Heidelberg University, the European Laboratory for Molecular Biology (EMBL), the German Cancer Research Center (DKFZ) and the Max-Planck-Institute for Medical Research, as well as with international partners. Our research activities are strengthened in particular by close interdisciplinary collaboration with scientists from the fields of physics, chemical biology, proteome and transcriptome analysis, cryo-electron microscopy, image analysis and scientific modelling.

More information on the research activities of the members of the Department of Infectious Diseases, the ZMBH-group and the associated research groups participating in this Major can be found in the profiles provided in the appendix and on the corresponding websites.

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".



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.

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.

Criteria for admission

We welcome appropriately qualified students from all over the world to this course. Since modern infectious disease research focuses on molecular mechanisms of pathogenesis, 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 mandatory. Students in the Heidelberg Bachelor courses "Biology" and "Molecular and Cellular Biology" who are

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

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 tropical medicine. There are five units with a large number of research groups, most of which are involved in the educational activities of this Major. These units are:

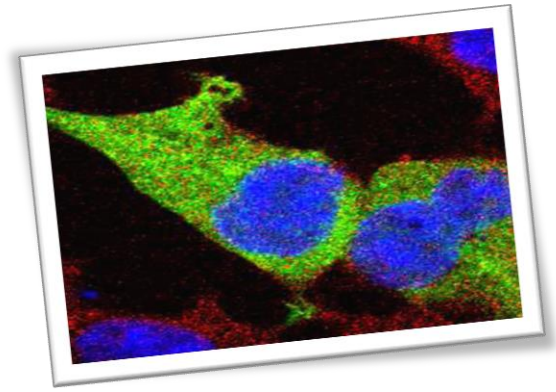
- Medical Microbiology and Hygiene
- Molecular Virology
- Virology
- Integrative Virology
- Parasitology

Medical Microbiology

Fields of Interest

Teams in the Medical Microbiology and Hygiene unit 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 research unit 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 research unit 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 research unit 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 (W3) 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 Stadt Krankenhaus Alfeld, Internal Medicine, License to practice medicine 1998: 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
- Microbiome of Cystic Fibrosis patients

Selected Publications

Boutin S, Graeber SY, Stahl M, Dittrich SA, Mall MA and Dalpke AH: Chronic but not intermittent infection with *Pseudomonas aeruginosa* is associated with global changes of the lung microbiome in cystic fibrosis. *Eur Respir J* 2017; in press

Zimmer J, Weitnauer M, Boutin S, Küblbeck G, Thiele S, Walker P, Lasitschka F, Lunding L, Orinska Z, Vock V, Arnold B, Wegmann M and Dalpke A: Nuclear localization of Suppressor of Cytokine Signaling (SOCS)-1 regulates local immunity in the lung. *Front. Immunol.* 2016; 7: 514, doi: 10.3389/fimmu.2016.00514

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 NFkB 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

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

Chakraborty S, Kloos B, Harre U, Schett G, Kubatzky KF: *Pasteurella multocida* Toxin Triggers RANKL-independent Osteoclastogenesis. *Front Immunol* **2017**; 8:185

Hildebrand D, Heeg K, Kubatzky KF: *Pasteurella multocida* Toxin Manipulates T Cell Differentiation. *Front Microbiol* **2015**; Nov 19; 6:1273

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**; Sep 14; 13:40

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, Kortzen 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

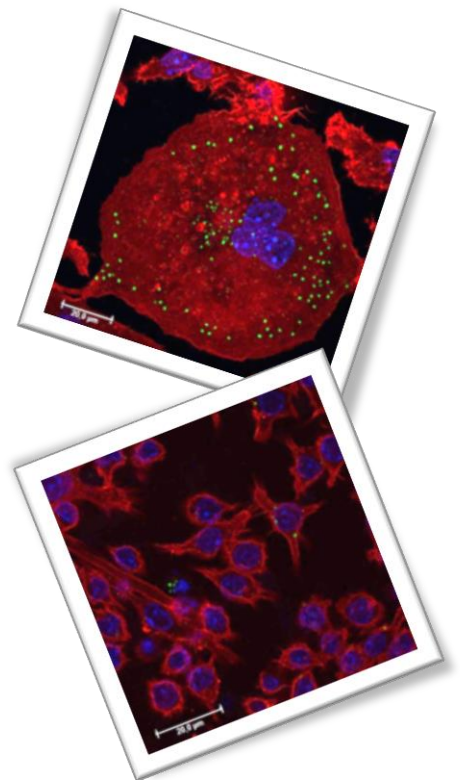
Hildebrand D, Sähr A, Wölfle SJ, Heeg K and Kubatzky KF: „Regulation of Toll-like receptor 4-mediated immune responses through *Pasteurella multocida* toxin-induced G protein signalling. *Cell Commun Signal* **2012**; 1;10(1): 22

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. IF 4.258

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

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

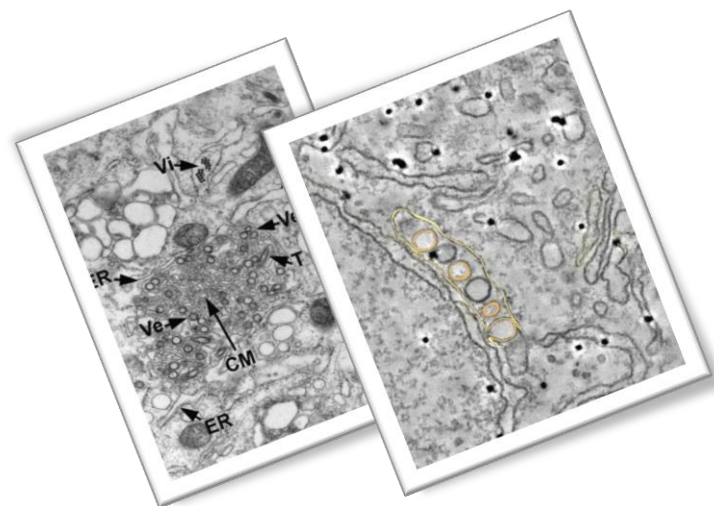


Molecular Virology

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) and several flaviviruses, most notably Dengue virus (DENV) and Zikavirus (ZIKV). These viruses are leading causes for death worldwide with about 400 million people suffering from a chronic infection with HBV or HCV and about 400 million new DENV infections occurring each year, especially in tropical countries. Moreover, the recent pandemic spread of ZIKV underscores the medical relevance of this virus family.

As a department that focuses on the molecular and cell biology of these infections, the following topics are studied: virus-host cell interactions, mechanism of host cell infection, morphology, biogenesis and dynamics of viral replication factories, virus assembly and involved host cell factors, viral and cellular factors and their suitability for (broad-spectrum) antiviral therapy, RNA structures and their role for viral replication, mathematical modeling and simulation of virus replication and interaction with innate immune responses, 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. In addition to



state-of-the-art methods in these fields we use live cell imaging, cutting edge light and electron microscopy as well as 3D reconstructions.

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 Department of Infectious Diseases, Molecular Virology, 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 (HBV, HCV DENV and ZIKV)
- Structural and functional aspects of viral RNA replication and assembly
- Viral and host targets for antiviral therapy
- Mathematical modeling of virus replication and spread as well as innate immune responses and viral countermeasures
- Strategies of viral persistence

Selected Publications

Chatel-Chaix L, Cortese M, Romero-Brey I, Bender S, Neufeldt CJ, Fischl W, Scaturro P, Schieber N, Schwab Y, Fischer B, Ruggieri A, Bartenschlager R: Dengue Virus Perturbs Mitochondrial Morphodynamics to

Dampen Innate Immune Responses. *Cell Host Microbe* 2016; 20(3):342-56

Seitz S, Iancu C, Volz T, Mier W, Dandri M, Urban S, Bartenschlager R: A Slow Maturation Process Renders Hepatitis B Virus Infectious. *Cell Host Microbe* 2016; 20(1):25-35

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

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 of 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

Lempp FA, Ni Y, Urban S: Hepatitis delta virus: insights into a peculiar pathogen and novel treatment options. **Nature Reviews Gastroenterology & Hepatology** 2016; 13(10):580-9

Bogomolov P, Alexandrov A, Voronkova N, Macievich M, Kokina K, Petrachenkova M, Lehr T, Lempp FA, Wedemeyer H, Haag M, Schwab M, Haefeli WE, Blank A, Urban S: Treatment of chronic hepatitis D with the entry inhibitor myrcludex B: First results of a phase Ib/IIa study. **J Hepatol.** 2016; pii: S0168-8278(16)30148-9.

Li W, Urban S: Entry of hepatitis B and hepatitis D virus into hepatocytes: Basic insights and clinical implications. **J Hepatol.** 2016; doi: 10.1016/j.jhep.2016.02.011

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

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

Harak C, Meyrath M, Romero-Brey I, Schenk C, Gondeau C, Schult P, Esser-Nobis K, Saeed M, Neddermann P, Schnitzler P, Gotthardt D, Perez-Del-Pulgar S, Neumann-Haefelin C, Thimme R, Meuleman P, Vondran FW, Francesco R, Rice CM, Bartenschlager R, Lohmann V: Tuning a cellular lipid kinase activity adapts hepatitis C virus to replication in cell culture. **Nat Microbiol.** 2016 Dec 19;2:16247.

Esser-Nobis K, Schmidt J, Nitschke K, Neumann-Haefelin C, Thimme R, Lohmann V: The cyclophilin-inhibitor alisporivir stimulates antigen presentation thereby promoting antigen-specific CD8(+) T cell activation. **J Hepatol.** 2016; 64(6):1305-14.

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

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

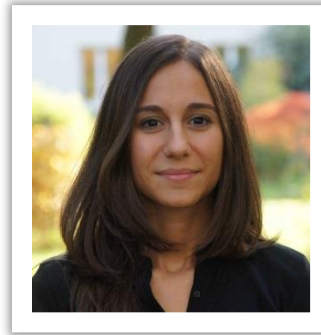
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inhibition of hepatitis C virus replication using a novel immunological model. **Gastroenterology** 2009; 136(4):1391-401

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 the host stress response to RNA virus infection

- Identification of regulators of hepatitis C virus-induced stress granule oscillation
- Mathematical modeling of oscillating host stress response to hepatitis C virus infection
- Interplay of Flaviviruses with the host cell translation machinery
- Innate immune sensing of human endogenous retroviruses

Selected Publications

Roth H, Magg V, Uch F, Mutz P, Klein P, Haneke K, Lohmann V, Bartenschlager R, Fackler OT, Locker N, Stoecklin G, Ruggieri A. Flavivirus infection uncouples translation suppression from cellular stress responses. **mBio** 2017; 8:e02150-16.

Cortese M, Goellner S, Acosta EG, Neufeldt CJ, Oleksiuk O, Lampe M, Haselmann U, Funaya C, Schieber N, Ronchi P, Schorb M, Pruunsild P, Schwab Y, Chatel-Chaix L, Ruggieri A, Bartenschlager R. Ultrastructural characterization of Zika virus replication factories. **Cell Reports** 2017, 18(9): 2113–2123.

Chatel-Chaix L, Cortese M, Romero-Brey I, Bender S, Fischl W, Scaturro P, Fischer B, Ruggieri A, Bartenschlager R. Dengue virus modulates mitochondrial morphodynamics through the inhibition of DRP-1 for the benefit of viral replication. **Cell Host Microbe** 2016; 20(3):342-56.

Trotart M, Tsopoulidis N, Tibroni N, Willemsen J, Binder M, Ruggieri A, Fackler OT. Sensing of HIV-1 infection in Tzm-bl cells with reconstituted expression of STING. **J Virol.** 2015; 90(4):2064-76.

Schmid B*, Rinas M*, Ruggieri A, Reuter A, Fischl W, Harder N, Bergeest J-P, Flossdorf M, Rohr K, Höfer T, Bartenschlager R. Live-cell analysis and modeling identify determinants of attenuation of Dengue virus 2-O-methyl mutant. **PLoS Pathog.** 2015; 11(12):e1005345.

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; 63(4):829-37.

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.

Ruggieri A, Maldener E, Sauter M, Müller-Lantzsch N, Meese E, Fackler O, Mayer J. Human endogenous retrovirus HERV-(HML-2) encodes a stable signal peptide with biological properties distinct from Rec. **Retrovirology** 2009; 6: 17.

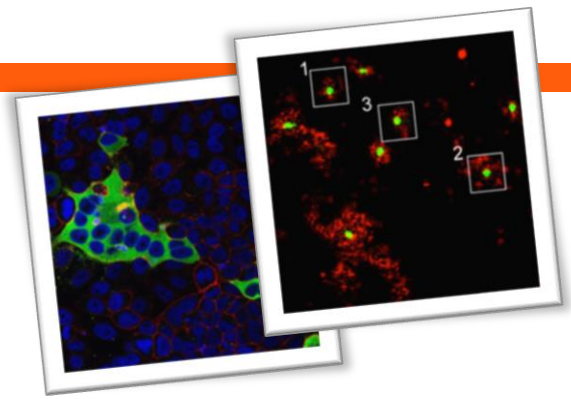
Virology

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, Schaller). In spite of several decades of intense 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 and the induction of the innate immune response. 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.

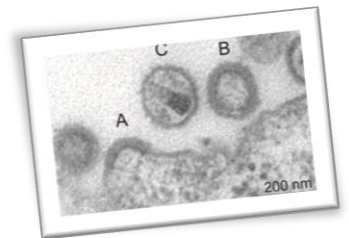
Other viral systems studied include parvoviruses, the enteropathogens norovirus and reovirus, bunyaviruses and influenza virus. We develop and use vectors based on adeno-associated virus for basic research and gene therapy approaches (Grimm) and exploit the CRISPR/Cas system for gene therapeutic and 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
- Dr. Torsten Schaller



Prof. Dr. Hans-Georg Kräusslich



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Scientific Vita

2014–present: Vice-dean for research Medical Faculty, Heidelberg University

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
- Innate response for HIV infection
- Transmission and therapy of HIV infection

Selected Publications

Mücksch F, Laketa V, Müller B, Schultz C, Kräusslich HG: Synchronized HIV assembly by tunable PIP2 changes reveals PIP2 requirement for stable Gag anchoring. *eLife* 2017; pii: e25287. doi: 10.7554/eLife.25287.

Mattei S, Glass B, Hagen WJ, Kräusslich HG, Briggs JA: The structure and flexibility of conical HIV-1 capsids determined within intact virions. *Science* 2016; 354(6318):1434-1437.

Hanne J, Göttfert F, Schimer J, Anders-Össwein M, Konvalinka J, Engelhardt J, Müller B, Hell SW, Kräusslich HG: Stimulated Emission Depletion Nanoscopy Reveals Time-Course of Human Immunodeficiency Virus Proteolytic Maturation. *ACS Nano* 2016; in press

Schur FK, Obr M, Hagen WJ, Wan W, Jakobi AJ, Kirkpatrick JM, Sachse C, Kräusslich HG, Briggs JA: An atomic model of HIV-1 capsid-SP1 reveals structures regulating assembly and maturation. *Science* 2016; 353(6298):506-8

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

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

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

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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

Movie:
<http://www.spektrum.de/video/partner/cellnetworks/virus-cell-interactions-brought-to-light/1471891>

Sakin V, Hanne J, Dunder J, Anders-Össwein M, Laketa V, Nikić I, Kräusslich HG, Lemke EA, Müller B: A Versatile Tool for Live-Cell Imaging and Super-Resolution Nanoscopy Studies of HIV-1 Env Distribution and Mobility. *Cell Chem Biol* 2017; 24: 635-645.e5

Sakin V, Paci G, Lemke E, Müller B: Labeling of virus components for advanced quantitative imaging analyses. *FEBS L* 2016; 590, 1896-1914

Hanne J, Göttfert F, Schimer J, Anders-Össwein M, Konvalinka J, Engelhardt J, Müller B, Hell SW, Kräusslich HG: Stimulated Emission Depletion Nanoscopy Reveals Time-Course of Human Immunodeficiency Virus Proteolytic Maturation. *ACS Nano* 2016; in press

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

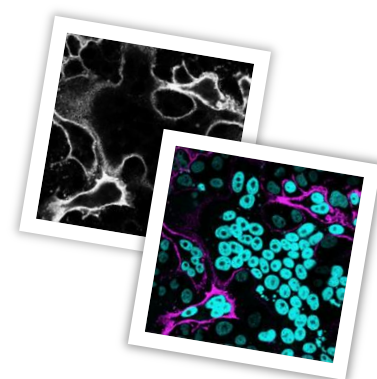
Schimer J, Pavova M, Anders M, Pachel P, Sacha P, Cigler P, Weber J, Majer P, Rezacova P, Kräusslich HG, Müller B***, Konvalinka J***: Triggering HIV polyprotein processing inside virions by rapid photodegradation of a tight-binding photodegradable protease inhibitor. *Nature Communications* 2015; 6:6461

Hendrix J, Baumgärtel V, Schimpf W, Ivanchenko S, Digan 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

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 subviral 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

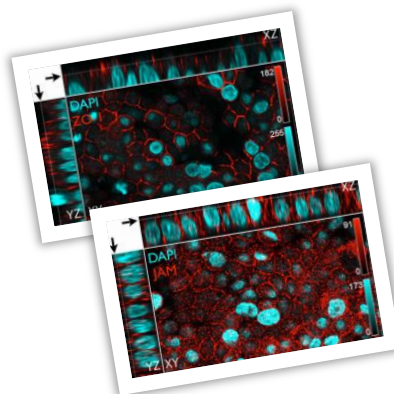
Kural C, Tacheva-Grigorova SK, Boulant S, Cocucci E, Baust T, Duarte D, Kirchhausen T: Dynamics of intracellular clathrin/AP1- and clathrin/AP3-containing carriers. **Cell Rep** 2012; 2(5):1111-9

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, Hacoen 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-dependent 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



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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) and bocaviral (BoV) vectors
- Gene/genome engineering (CRISPR, TALENs)
- RNA interference (RNAi)

- Induced pluripotent stem cells (iPSC)
- Synthetic biology

Selected Publications

Senís E, Mockenhaupt S, Rupp D, Bauer T, Paramasivam N, Knapp B, Gronych J, Grosse S, Windisch MP, Schmidt F, Theis FJ, Eils R, Lichter P, Schlesner M, Bartenschlager R, Grimm D: TALEN/CRISPR-mediated engineering of a promoterless anti-viral RNAi hairpin into an endogenous miRNA locus. *Nucleic Acids Res* **2016**; in press

Michler T, Grosse S, Mockenhaupt S, Röder N, Stückler F, Knapp B, Ko C, Heikenwälder M, Protzer U, Grimm D: Blocking sense strand activity improves potency, safety and specificity of anti-hepatitis B virus short hairpin RNA. *EMBO Mol Med* **2016**; 8:1082-98

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, Streez 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:e1399

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, Streez 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

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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

Mazelier M, Rouxel RN, Zumstein M, Mancini R, Bell-Sakyi L and Lozach PY: Uukuniemi virus as a tick-borne virus model. *J Virol* **2016**; 90:6784-98

Albornoz A, Hoffmann AB, Lozach PY and Tischler ND: Early bunyavirus-host cell interactions. *Viruses* **2016**; 8:143

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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

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Scientific Vita

2015-present: Junior group leader, Center of Infectious Diseases, Heidelberg University

2014-2015: Junior group leader, Institute for Medical Virology, Goethe University Frankfurt

2011-2014: PostDoc, Prof Michael Malim, Department of Infectious Diseases, King's College London, UK

2009-2011: PostDoc, Prof Greg Towers, Centre for Medical Molecular Virology, University College London, UK

2005-2009: PhD, Prof Greg Towers, University College London, UK

2000-2005: Diploma, Prof Ralf Bartenschlager, Heidelberg University

Specific Research Interests

- Molecular virology
- Cell biology of virus infection
- HIV-1 early infection events and host dependency factors
- Resistance and restriction factors
- Interferon-induced block to HIV-1 infection
- Innate immunity and sensing of pathogens
- Peptidylprolyl cis-trans isomerases in HIV-1 biology

Selected Publications

Bulli L, Apolonia L, Kutzner J, Pollpeter D, Goujon C, Herold N, Schwarz SM, Giernat Y, Keppler OT, Malim MH, Schaller T: Complex Interplay between HIV-1

Capsid and MX2-Independent Alpha Interferon-Induced Antiviral Factors. *J Virol* **2016**; 90:7469-7480

Schaller T, Herold N: The Early Bird Catches the Worm - Can Evolution Teach us Lessons in Fighting HIV? *Curr HIV Res* **2016**; 14:183-210

Fletcher AJ, Christensen DE, Nelson C, Tan CP, Schaller T, Lehner PJ, Sundquist WI, Towers GJ: TRIM5alpha requires Ube2W to anchor Lys63-linked ubiquitin chains and restrict reverse transcription. *EMBO J* **2015**; 34:2078-2095

Schaller T, Pollpeter D, Apolonia L, Goujon C, Malim MH: Nuclear import of SAMHD1 is mediated by a classical karyopherin alpha/beta1 dependent pathway and confers sensitivity to VpxMAC induced ubiquitination and proteasomal degradation. *Retrovirology* **2014**; 11:29

Goujon C, Moncorge O, Bauby H, Doyle T, Ward CC, Schaller T, Hue S, Barclay WS, Schulz R, Malim MH: Human MX2 is an interferon-induced post-entry inhibitor of HIV-1 infection. *Nature* **2013**; 502:559-562

Schaller T, Goujon C, Malim MH: AIDS/HIV. HIV interplay with SAMHD1. *Science* **2012**; 335:1313-1314

Price AJ, Fletcher AJ, Schaller T, Elliott T, Lee K, KewalRamani VN, Chin JW, Towers GJ, James LC: CPSF6 defines a conserved capsid interface that modulates HIV-1 replication. *PLoS pathogens* **2012**; 8:e1002896

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Schaller T, Hue S, Towers GJ: An active TRIM5 protein in rabbits indicates a common antiviral ancestor for mammalian TRIM5 proteins. *J Virol* **2007**; 81:11713-11721

Schaller T, Appel N, Koutsoudakis G, Kallis S, Lohmann V, Pietschmann T, Bartenschlager R: Analysis of hepatitis C virus superinfection exclusion by using novel fluorochrome gene-tagged viral genomes. *J Virol* **2007**; 81:4591-4603

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 mechanisms 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 and virus replication/pathogenesis. These analyses are preferentially conducted 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.

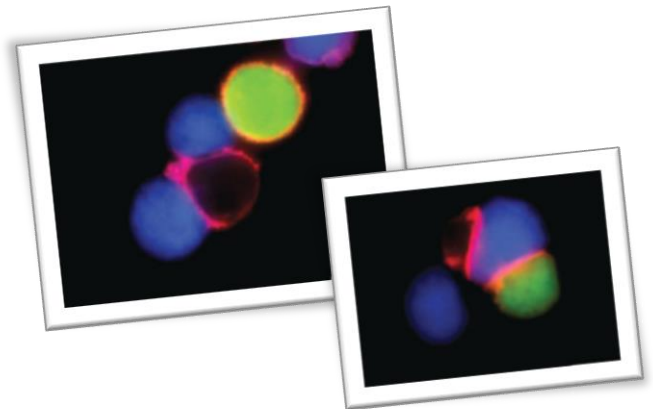
While an overall goal of our laboratory is to explore the specific contributions of nuclear topology and chromatin factors to HIV integration site selection and establishment of latency, we are specifically interested in determining the role of nuclear pore complex proteins in integration site selection. 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



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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 intrinsic immunity against HIV-1 and viral evasion thereof
- HIV accessory genes

Selected Publications

Pujol FM, Laketa V, Schmidt F, Mukenhirn M, Müller B, Boulant S, Grimm D, Keppler OT and Fackler OT: HIV-1 Vpu Antagonizes CD317/tetherin by Adaptor protein-1-Mediated Exclusion from Virus Assembly Sites. *J Virol* **2016**; 90:6709-6723.

Imle A, Abraham L, Tsopoulidis N, Hoflack B, Saksela K and Fackler OT: Association with PAK2 Enables Functional Interactions of Lentiviral Nef Proteins with Exocyst. *mBio* **2015**; 6: e01309-15

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

Kutscheid S, Zhu R, Antoku S, Luxton GGW, Stagljär I, Fackler OT, 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, 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

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

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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 upon viral infection
- Control of HIV-1 integration and cellular fate

- HIV-1 transcription and latency; role of oxidative stress

Selected Publications

Lusic M and Robert F. Siliciano: Nuclear landscape of HIV-1 infection and integration. *Nat Rev Microb* **2016**; (in press)

Lucic B and Lusic M: Connecting HIV-1 integration and transcription: a step toward new treatments. *FEBS Letters* **2016**; 590 (13):1927

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**; 14;521(7551):227-31

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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

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

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 214 million clinical cases and killing approximately 438,000 people every year (WHO, 2015). 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 development 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.

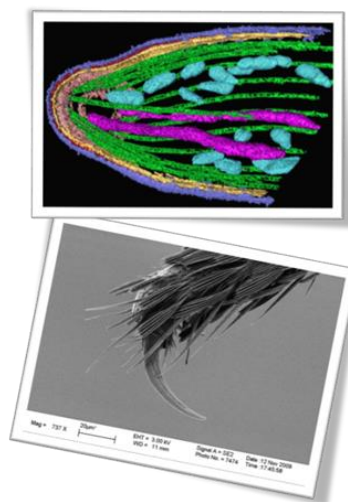
Malaria research conducted by the Parasitology Unit includes the following aspects:

The Lanzer lab addresses key questions related to the molecular and biophysical mechanisms underpinning cytoadhesion of *Plasmodium falciparum*-infected erythrocytes. *P. falciparum* is the most virulent of the 5 *Plasmodium* species that can cause malaria in humans. The group is further interested in understanding how genetic polymorphisms in the human genome, such as those leading to sickle cell haemoglobin or haemoglobin C protect carriers from severe malaria-related disease and death. Another research focus concerns mechanisms of drug resistance and strategies to overcome established resistance mechanisms, including the development of novel antimalarial drugs.

The Frischknecht lab studies the formation and motility of the sporozoite and the intracellular development within the liver using a mix of reverse genetics, imaging and biophysical approaches. Studies are mainly performed using rodent malaria parasites, which can be easier manipulated than the human parasites. The group has many collaboration partners on the Heidelberg campus and around the world.

The Ganter lab investigates the unusual way in which the malaria parasite *Plasmodium* replicates. Cells usually divide themselves into two daughter cells; however, *Plasmodium* forms multinucleated cells, within which nuclei autonomously divide before daughter cells are formed. Using various techniques—including reverse genetics, advanced imaging, and proteomic approaches—the group uses human and rodent malaria parasites to gain insight into the molecular mechanisms that drive this non-canonical replication cycle.

The Guizetti lab studies the unusual cell division mechanisms of the malaria parasite *Plasmodium falciparum*. Rapid mitotic divisions enable proliferation of the parasite in the human blood cells and contribute to disease severity. Even though mitosis in this parasite shows significant differences to what has been described in classical model organisms, it is poorly studied so far. We use super-resolution, electron, and live cell microscopy technologies combined with CRISPR/Cas9 genome editing to describe the dynamics and regulation of chromosomes, centromeres, and the nuclear envelope during division. Thereby we hope to uncover new targets within this essential pathway and contribute to the fight against malaria.



The Mueller team is fascinated by the prospect of using a better understanding of the malaria host-pathogen interaction to investigate new intervention strategies that would ultimately allow for the development of a malaria vaccine. Complete or partial inhibition of malaria parasite replication in the liver represents a powerful approach for preventing malarial disease. This clinically silent phase of the *Plasmodium* life cycle has often been overlooked by malaria researchers due to its limited accessibility – this has indeed completely changed over the last few years. Hence the Mueller laboratory investigates this stage of the malaria parasite with two ultimate goals: identifying novel targets for a next-generation anti-infective vaccine and understanding the parasite-host interaction for potential other means of interventions such as drug development. Based on our experiences in applied microbiology, cell biology, parasitology, immunology the major focus of the Mueller laboratory is a combined approach between genetics, cell biology and immunology in *Plasmodium* parasites. The group is equipped with the first-in-house insectary for both *P. berghei* and *P. falciparum* mosquito infections allowing the team to study all different stages of the complex malaria life cycle in vivo as well as in vitro.

The Portugal lab aims to explore the biology of asymptomatic *P. falciparum* parasites and its interactions with the human host during the dry season that ensure that the parasite is not cleared and can be transmitted in the next transmission season. The main interests are: 1) Compare the properties and function of *P. falciparum* parasites from asymptomatic individuals during the dry season versus symptomatic individuals during the malaria season; 2) Determine the kinetics of gametocyte carriage throughout the dry season; and 3) Scrutinize internal signals and/or environmental cues promoting proliferation and gametocytogenesis when the mosquito vector returns during the rainy season.

The Przyborski lab studies how the malaria parasite *P. falciparum* modifies its host cell, the mature human erythrocyte. In particular, the group is interested in the role of a large number of proteins that the parasite synthesizes and transports to the erythrocyte, and which themselves are involved in further modification of the infected cell. Of particular interest is an expanded family of Dnaj/Hsp40-like proteins that is likely to be important for the transport of virulence factors to the surface of the infected red-blood cell. Additional exported proteins, although important for parasite survival, have no counterparts in other biological systems, and may thus potentially be targeted by future generations of antimalarials. With the eventual goal of identifying potential future drug-targets, and in collaboration with other researchers in Heidelberg and around the world, the group combines a diverse array of cell biology, genetic and biochemical techniques.

The Osier lab works to identify the antibody targets of naturally acquired immunity against *Plasmodium falciparum* malaria and the antibody-dependent mechanisms that underlie protective immunity. The group also seeks to understand how parasite diversity is overcome in immune persons facing natural challenge, and to test the efficacy of combination malaria vaccines. The group aims to contribute to the development of highly effective vaccines against malaria using the model of naturally acquired protective immunity.

The following teams belong to the Parasitology Unit:

- Prof. Dr. Michael Lanzer (Head of the Parasitology Unit)
- Prof. Dr. Friedrich Frischknecht
- Dr. Markus Ganter
- Dr. Julien Guizetti
- Dr. Ann-Kristin Mueller
- Dr. Silvia Portugal
- Dr. Faith Osier
- Dr. Jude Przyborski

Prof. Dr. Michael Lanzer



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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, Bisseze C, Simapore 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

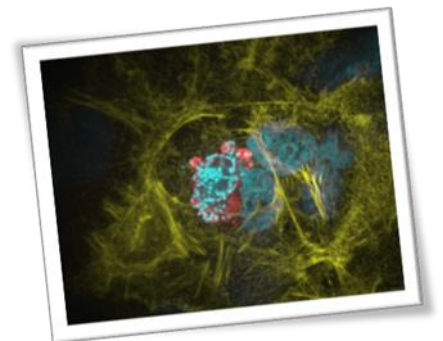
STEVOR to the Maurer's clefts in *Plasmodium falciparum*-infected erythrocytes. **Embo J** 2005; 24: 2306-2317

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

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

Bane K, Lepper S, Kehrer J, Sattler J, Singer M, Reinig M, Heiss K, Baum J, Mueller AK and Frischknecht F: The actin filament-binding protein coronin regulates motility in *Plasmodium* sporozoites. **PLoS Pathogens** 2016; 12, e1005710

Quadt K, Streichfuss M, Moreau C, Spatz JP, Frischknecht F: Coupling of retrograde flow to force production during malaria parasite migration. **ACS Nano** 2016; 10, 2091-2102

Singer M, Marshall J, Heiss K, Mair GR, Grimm D, Mueller AK and Frischknecht F: Zinc-finger nuclease-based double strand breaks attenuate malaria parasites and reveal rare micro-homology mediated end joining. **Genome Biology** 2015; 16, 249, 2015

Douglas RG, Amino R, Sinnis P, Frischknecht F: Active migration and passive transport of malaria parasites. **Trends Parasitol** 2015; 34,357-62

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

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

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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

2016-present: Junior Group Leader, Department of Infectious Diseases, Parasitology, Heidelberg University Hospital, Heidelberg

2010-2016: PostDoc, Harvard University, Cambridge, MA, USA

2009-2010: PostDoc, Max Planck Institute for Infection Biology, Berlin

2005-2009: PhD student, Department of Infectious Diseases, Parasitology, Heidelberg University Hospital, Heidelberg

2000-2005: Studies of Biology, Heidelberg University, Heidelberg

Specific Research Interests

- molecular parasitology
- malaria cell biology of replication
- cell cycle regulation
- reverse genetics and inducible knockdown technology
- advanced imaging and proteomics

Selected Publications

Ganter M, Goldberg JM, Dvorin JD, Paulo JA, King JG, Tripathi AK, Paul AS, Yang J, Coppens I, Jiang RHY, Baker DA, Dinglasan RR, Gygi SP, Duraisingh MT. *Plasmodium falciparum* CRK4 directs continuous rounds of DNA replication during schizogony. **Nature Microbiology** 2017; 2, 17017

Paul AS, Saha S, Jiang RHY, Coleman BI, Kosber AL, Chen C, Ganter M, Espy N, Gubbels MJ, Duraisingh MT. Parasite calcineurin regulates host cell recognition and attachment by apicomplexans. **Cell Host Microbe** 2015; 18, 49-60

Ganter M, Rizopoulos Z, Schuler H, Matuschewski K. 2015. Pivotal and distinct role for *Plasmodium* actin capping protein alpha during blood infection of the Malaria parasite. **Molecular Microbiology** 2015; 96, 84-94

Coleman BI, Skillman KM, Jiang RHY, Childs LM, Altenhofen LM, Ganter M, Leung Y, Goldowitz I, Kafsack BFC, Marti M, Llinas M, Buckee CO, Duraisingh MT. A *Plasmodium falciparum* histone deacetylase regulates antigenic variation and gametocyte conversion. **Cell Host Microbe** 2014; 16, 177-186

Sattler J#, Ganter M#, Hliscs M, Matuschewski K, Schuler H. 2011. Actin regulation in the malaria parasite. **European Journal of Cell Biology** 2011; 90, 966-971

Siden-Kiamos I#, Ganter M#, Kunze A, Hliscs M, Steinbüchel M, Mendoza J, Sinden R, Louis K, Matuschewski K. Stage-specific depletion of myosin A supports an essential role in motility of malarial ookinetes. **Cellular Microbiology** 2011; 13, 1996-2006

Ganter M, Schuler H, Matuschewski K. Vital role for the *Plasmodium* capping protein (CP) beta subunit in motility of malaria sporozoites. **Molecular Microbiology** 2009; 74, 1356-1367

Kursula I, Kursula P, Ganter M, Panjikar S, Matuschewski K, Schuler H. Structural basis for

parasite-specific functions of the divergent profilin of *Plasmodium falciparum*. **Structure** 2008; 16, 1638-1648

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Scientific Vita

2017-present: Young group leader at Heidelberg University Hospital investigating nuclear division mechanisms in human malaria parasites.

2017: Visiting researcher at Siegel lab, University Würzburg (Germany).

2011-2016: Postdoc as HFSP fellow Scherf lab, Institut Pasteur, Paris (France).

2011: One-month volunteering project, Sironko, (Uganda).

2007-2011: PhD project at Gerlich lab, ETH Zurich (Switzerland).

2006: Diploma thesis project at Vogel lab, McGill University, Montreal (Canada).

2003 – 2005: Studies in Biotechnology, ESBS university, Strasbourg (France).

2001 – 2003: Studies in Biology, University Karlsruhe (Germany).

Specific Research Interests

- Molecular parasitology
- Cell division mechanisms of malaria parasite
- Cellular dynamics of mitotic factors
- Super-resolution and electron microscopy methods
- Genome editing of human blood stage malaria parasites
- Host-pathogen interactions and antigenic variation

Selected Publications

Bryant J.M., Regnault C., Scheidig-Benatar C., Baumgarten S., Guizetti J.*, Scherf A.. CRISPR/Cas9 Genome Editing Reveals That the Intron Is Not Essential for var2csa Gene Activation or Silencing in *Plasmodium falciparum*. **MBio** 2017; 8(4) pii: e00729-17.

Guizetti, J.*, Barcons-Simon, A., Scherf, A. Transacting GC-rich non-coding RNA at var expression site modulates gene counting in malaria parasite. **Nucleic Acids Res** 2016; 44, 9710–9718.

Zhang, Q., Siegel, T. N., Martins, R.M., Wang, F., Cao, J., Gao, Q., Cheng, X., Jiang, L., Hon, C. C., Scheidig-Benatar, C., Sakamoto, H., Turner, L., Jensen, A. T., Claes, A., Guizetti, J., Malmquist, N. A., and Scherf, A.. Exonuclease-mediated degradation of nascent RNA silences genes linked to severe malaria. **Nature** 2014, 513, 431-435.

Guizetti, J., Martins, R.M., Guadagnini, S., Claes, A., and Scherf, A. Nuclear Pores and Perinuclear Expression Sites of var and Ribosomal DNA Genes Correspond to Physically Distinct Regions in *Plasmodium falciparum*. **Eukaryot Cell** 2013; 12, 697-702.

Guizetti, J.*, and Scherf, A. Silence, activate, poise and switch! Mechanisms of antigenic variation in *Plasmodium falciparum*. **Cell Microbiol** 2013;15, 718-726.

Guizetti, J., Schermelleh, L., Mantler, J., Maar, S., Poser, I., Leonhardt, H., Muller-Reichert, T., and Gerlich, D. W. Cortical constriction during abscission involves helices of ESCRT-III-dependent filaments. **Science** 2011; 331, 1616-1620.

Guizetti, J., Mantler, J., Muller-Reichert, T., and Gerlich, D.W. Correlative time-lapse imaging and electron microscopy to study abscission in HeLa cells. **Methods Cell Biol** 2010; 96, 591-601.

Guizetti, J., and Gerlich, D.W. Cytokinetic abscission in animal cells. **Semin Cell Dev Biol** 2010; 21, 909-916.

Steigemann, P., Wurzenberger, C., Schmitz, M.H., Held, M., Guizetti, J., Maar, S., and Gerlich, D.W. Aurora B-mediated abscission checkpoint protects against tetraploidization. **Cell** 2009; 136, 473-484.

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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 Heidelberg Akademie der Wissenschaften

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

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

Sá e Cunha C., Nyboer B., Heiss K., Sanches-Vaz M., Fontinha D., Wiedtke E., Grimm D., Przyborski JM., Mota MM., Prudêncio M., Mueller AK. P.berghei EXP-1 interacts with host Apolipoprotein H during *Plasmodium* liver-stage development. **Proc Natl Acad Sci U S A.** 2017; pii: 201606419. doi: 10.1073/pnas.1606419114

Hoffmann A, Pfeil J, Alfonso J, Kurz FT, Sahm F, Heiland S, Monyer H, Bendszus M, Mueller AK, Helluy X, Pham M: Experimental cerebral malaria spreads along the rostral migratory stream. **PLOS Pathog** 2016; 12(3):e1005470

Lewis MD, Behrends J, Sa e Cunha C, Mendes A, Lasitschka F, Sattler JM, Heiss K, Kooij T, Prudencio M, Bringmann G, Frischknecht F, Mueller AK: Chemical attenuation of *Plasmodium* in the liver

modulates severe malaria disease progression. *J Immunol* 2015; 14,00863

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 approved 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

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

2016-present: Group leader Parasitology, Heidelberg University Hospital

2011-2016: Posdoc (NIAID, NIH, USA)

2010: FAPESP Invited Visiting Researcher (Universidade de São Paulo, Brazil)

2005-2010: PhD thesis (Faculdade de Medicina da Universidade de Lisboa, Portugal)

1998-2003: Biology undergraduate (Faculdade de Ciência da Universidade do Porto, Portugal)

Specific Research Interests

- Compare the transcriptional profile, the metabolic activity, and functional properties of Pf parasites freshly isolated from asymptomatic individuals during the dry season versus symptomatic individuals during the malaria season.
- Determine the kinetics of gametocyte carriage throughout the dry season.
- Evaluate the transmission capacity of parasites kept asymptotically during the dry season.

Selected Publications

Krishnamurthy AT, Thouvenel T, Portugal S, Keitany G, Hondowicz BD, Kim K, Holder A, Crompton PD, Rawlings D, Pepper M: Somatically hypermutated *Plasmodium*-specific IgM+ memory B cells are rapid, plastic first responders to a secondary malaria infection. *Immunity*; in press

Obeng-Adjei N, Portugal S, Tran TM, Yazew TB, Skinner J, Li S, Jain A, Felgner PL, Doumbo OK, Kayentao K, Ongoiba A, Traore B, Crompton PD: Circulating Th1-Cell-type Tfh Cells that Exhibit Impaired B Cell Help Are Preferentially Activated during Acute Malaria in Children. *Cell Rep* 2015; 13(2):425-39

Arama C, Skinner J, Doumbo D, Portugal S, Tran TM, Jain A, Traore B, Doumbo OK, Davies DH, Troye-Blomberg M, Dolo A, Felgner PL, Crompton PD: Genetic Resistance to Malaria Is Associated With Greater Enhancement of Immunoglobulin (Ig)M Than IgG Responses to a Broad Array of *Plasmodium falciparum* Antigens. *Open Forum Infect Dis* 2015; 26;2(3):ofv118

Portugal S, Tipton CM, Sohn H, Kone Y, Wang J, Li S, Skinner J, Virtaneva K, Sturdevant DE, Porcella SF, Doumbo OK, Doumbo S, Kayentao K, Ongoiba A, Traore B, Sanz I, Pierce SK, Crompton PD: Malaria-associated atypical memory B cells exhibit markedly reduced B cell receptor signaling and effector function. *Elife*. 2015; May 8;4. PMID: 25955968

Subramaniam KS, Skinner J, Ivan E, Mutimura E, Kim RS, Feintuch CM, Portugal S, Anastos K, Crompton PD, Daily JP: HIV Malaria Co-Infection Is Associated with Atypical Memory B Cell Expansion and a Reduced Antibody Response to a Broad Array of *Plasmodium*

falciparum Antigens in Rwandan Adults. *PLoS One* 2015; 10(4):e0124412

Banga S, Coursen JD, Portugal S, Tran TM, Hancox L, Ongoiba A, Traore B, Doumbo OK, Huang CY, Harty JT, Crompton PD: Impact of acute malaria on pre-existing antibodies to viral and vaccine antigens in mice and humans. *PLoS One* 2015; 10(4):e0125090

Bahtiyar Y, Portugal S, Tran TM, Gozzelino R, Ramos S, Gomes J, Regalado A, Cowan PJ, d'Apice AJF, Chong AS, Doumbo OK, Traore B, Crompton PD, Silveira H, Soares MP: Gut Microbiota Elicits a Protective Immune Response Against Malaria Transmission. *CELL* 2014; 159(6):1277-89

Portugal S, Moebius J, Skinner J, Doumbo D, Doumbo D, Kone Y, Dia S, Kanakabandi K, Sturdevant DE, Virtaneva K, Porcella SF, Li S, Doumbo OK, Kayentao K, Ongoiba A, Traore B, Crompton PD: Exposure-dependent control of malaria-induced inflammation in children. *PLoS Pathog.* 2014; 10(4):e1004079

Portugal S, Doumbo D, Traore B, Miller LH, Troye-Blomberg M, Doumbo OK, Dolo A, Pierce SK, Crompton PD: B cell analysis of ethnic groups in Mali with differential susceptibility to malaria. *Malar J* 2012; 11(1):162

Portugal S, Carret C, Recker M, Armitage AE, Gonçalves LA, Epiphanyo S, Sullivan D, Roy C, Newbold CI, Drakesmith H and Mota MM: Host mediated regulation of superinfection in malaria. *Nat Med* 2011; (6):732-7

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Scientific Vita

2017: Heisenberg Fellow and Senior Group Leader, Centre for Infectious Disease, University Hospital Heidelberg, Germany.

2013: apl. Prof., University of Marburg, Germany

2010: Habilitation in Parasitology and Cell Biology, University of Marburg, Germany

2005: Group Leader, Department of Parasitology, University of Marburg, Germany

2004: PhD Molecular Parasitology, Liverpool School of Tropical Medicine, UK and University Hospital Heidelberg, Germany.

2000: BSc Human Science, University College London, UK

Specific Research Interests

- Malaria
- Chaperones
- Evolution
- Protein traffic
- Protein folding

Selected Publications

Meyer C, Barniol L, Hiss JA, Przyborski JM. The N-terminal extension of the P. falciparum GBP130 signal peptide is irrelevant for signal sequence function. *Int J Med Microbiol.* 2017 Jul 17.

Zhang Q, Ma C, Oberli A, Zinz A, Engels S, Przyborski JM. Proteomic analysis of exported chaperone/co-chaperone complexes of P. falciparum reveals an array of complex protein-protein interactions. *Sci Rep.* 2017 Feb 20;7:42188.

Rhiel M, Bittl V, Tribensky A, Charnaud SC, Strecker M, Müller S, Lanzer M, Sanchez C, Schaeffer-Reiss C, Westermann B, Crabb BS, Gilson PR, Külzer S, Przyborski JM. Trafficking of the exported P. falciparum chaperone PfHsp70x. *Sci Rep.* 2016 Nov 8;6:36174.

Tribensky A, Graf AW, Diehl M, Fleck W, Przyborski JM. Trafficking of PfExp1 to the parasitophorous vacuolar membrane of Plasmodium falciparum is independent of protein folding and the PTEX translocon. *Cell Microbiol.* 2017 May;19(5).

Heiny SR, Pautz S, Recker M, Przyborski JM. Protein Traffic to the Plasmodium falciparum apicoplast: evidence for a sorting branch point at the Golgi. *Traffic.* 2014 Dec;15(12):1290-304.

Külzer S, Charnaud S, Dagan T, Riedel J, Mandal P, Pesce ER, Blatch GL, Crabb BS, Gilson PR, Przyborski JM. Plasmodium falciparum-encoded exported hsp70/hsp40 chaperone/co-chaperone complexes within the host erythrocyte. *Cell Microbiol.* 2012 Nov;14(11):1784-95.

Külzer S, Rug M, Brinkmann K, Cannon P, Cowman A, Lingelbach K, Blatch GL, Maier AG, Przyborski JM. Parasite-encoded Hsp40 proteins define novel mobile structures in the cytosol of the P. falciparum-infected erythrocyte. *Cell Microbiol.* 2010 Oct;12(10):1398-420.

Gehde N, Hinrichs C, Montilla I, Charpian S, Lingelbach K, Przyborski JM. Protein unfolding is an essential requirement for transport across the parasitophorous vacuolar membrane of Plasmodium falciparum. *Mol Microbiol.* 2009 Feb;71(3):613-28.

Przyborski JM, Miller SK, Pfahler JM, Henrich PP, Rohrbach P, Crabb BS, Lanzer M. Trafficking of STEVOR to the Maurer's clefts in Plasmodium falciparum-infected erythrocytes. *EMBO J.* 2005 Jul 6;24(13):2306-17.

Przyborski J, Lanzer M. Parasitology. The malarial secretome. *Science.* 2004 Dec 10;306(5703):1897-8.

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Scientific Vita

2016-2021: Junior Group Leader, Department of Parasitology, University of Heidelberg

2013-present: Clinical Research Fellow and Group Leader, Biosciences Dept, KEMRI-Wellcome Trust Research Program (KWTRP), Kenya

2010-2012: Postdoc, Burnet Institute for Medical Research, Melbourne, Australia

2008-2010: Clinical Fellow in Immunology, Centre for Vaccinology and Tropical Medicine, Oxford, UK and KWTRP

2004-2008: Wellcome Trust Training Fellow (PhD), London School of Hygiene and Tropical Medicine and KWTRP

2003-2004: Masters in Human Immunity (with Distinction), University of Liverpool, UK

2001-2003: Member of the Royal College of Paediatrics and Child Health (MRCPCH), UK

1997-2003: Training in Paediatrics, KWTRP and National Health Service, UK

1990-1996: Bachelor of Medicine and Surgery, University of Nairobi, Kenya

Specific Research Interests

- Human immunity to Plasmodium falciparum malaria
- Parasite-host interactions
- Vaccine Development for malaria
- Epidemiology & Molecular biology of infectious diseases

Selected Publications

Murungi LM, Sondén K, Llewellyn D, Rono J, Guleid F, Williams AR, Ogada E, Thairu A, Färnert A, Marsh K, Draper SJ, Osier FH: Severe Plasmodium falciparum malaria: targets and mechanisms associated with protection in Kenyan children. *Infect Immun* 2016; 84: 950-63

Rono J, Färnert A, Murungi L, Ojal J, Kamuyu G, Guleid F, Nyangweso G, Wambua J, Kitsao B, Olotu A, Marsh K, Osier FH: Multiple clinical episodes of Plasmodium falciparum malaria in a low transmission intensity setting: exposure versus immunity. *BMC Med* 2015; 13: 114

Boyle MJ, Reiling L, Feng G, Langer C, Osier FH, Aspeling-Jones H, Cheng YS, Stubbs J, Tetteh KK, Conway DJ, McCarthy JS, Muller I, Marsh K, Anders RF, Beeson JG: Human Antibodies Fix Complement to Inhibit Plasmodium falciparum Invasion of Erythrocytes and Are Associated with Protection against Malaria. *Immunity* 2015; 42: 580-90

Osier FH, Mackinnon MJ, Crosnier C, Fegan G, Kamuyu G, Wanaguru M, Ogada E, McDade B, Rayner JC, Wright GJ, Marsh K: New antigens for a multicomponent blood-stage malaria vaccine. *Sci Transl Med* 2014; 6: 247ra102

Osier FHA, Feng G, Boyle MJ, Langer C, Zhou J, Richards JS, McCallum FJ, Reiling L, Jaworowski A, Anders R, Marsh K, Beeson JG: Opsonic phagocytosis of Plasmodium falciparum merozoites: mechanism in human immunity and a correlate of protection against malaria. *BMC Med* 2014; 12: 108

Murungi LM, Kamuyu G, Lowe B, Bejon P, Theisen M, Kinyanjui SM, Marsh K, Osier FH. A threshold concentration of anti-merozoite antibodies is required for protection from clinical episodes of malaria. *Vaccine* 2013; 31: 3936-42

Douglas AD, Williams AR, Illingworth JJ, Kamuyu G, Biswas S, Goodman AL, Wyllie DH, Crosnier C, Miura K, Wright GJ, Long CA, Osier FH, Marsh K, Turner AV, Hill AV, Draper SJ: The blood-stage malaria antigen PfRH5 is susceptible to vaccine-inducible cross-strain neutralizing antibody. *Nat Commun* 2011; 2: 601

Osier FHA, Weedall GD, Verra F, Murungi L, Tetteh KKA, Bull P, Faber BW, Remarque E, Thomas A, Marsh K, Conway DJ: Allelic diversity and naturally acquired allele-specific antibody responses to Plasmodium falciparum apical membrane antigen 1 in Kenya. *Infect Immun* 2010; 78: 4625-33

Osier FHA, Murungi LM, Fegan G, Tuju J, Tetteh KK, Bull PC, Conway DJ, Marsh K: Allele-specific antibodies to Plasmodium falciparum merozoite surface protein-2 and protection against clinical malaria. *Parasite Immunol* 2010; 32: 193-201

Osier FHA, Fegan G, Polley SD, Murungi L, Verra F, Tetteh KKA, Lowe B, Mwangi T, Bull PC, Thomas AW,

Cavanagh DR, McBride JS, Lanar DE, Mackinnon M, Conway DJ, Marsh K: Breadth and magnitude of antibody responses to multiple *Plasmodium falciparum* merozoite antigens are associated with protection from clinical malaria. *Infect Immun* 2008; 76: 2240-8

Prof. Dr. Christine Clayton



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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
- Control of mRNA splicing in trypanosomes
- Identification of the modes of action of compounds that kill trypanosomes, but not mammalian cells

Selected Publications

Antwi E, Haanstra J, Ramasamy G, Jensen B, Droll D, Rojas F, Minia I, Terrao M, Mercé C, Matthews K, Myler PJ, Parsons M and Clayton C: Integrative analysis of the *Trypanosoma brucei* gene expression cascade predicts differential regulation of mRNA processing and unusual control of ribosomal protein expression. *BMC Genomics* 2016; 17, 306, 10.1186/s12864-016-2624-3

Minia I, Clayton C: Regulating a post-transcriptional regulator: protein phosphorylation, degradation and translational blockage in control of the trypanosome stress-response RNA-binding protein ZC3H11. *PLoS Pathogens* 2016; 12, e1005514, 10.1371/journal.ppat.1005514

Mulindwa J, Mercé C, Matovu E, Enyaru J, Clayton C: Transcriptomes of newly-isolated *Trypanosoma brucei* rhodesiense reveal hundreds of mRNAs that are co-regulated with stumpy-form markers. *BMC Genomics* 2015; 16, 1118

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

Fadda A, Ryten M, Droll D, Rojas F, Färber V, Haanstra JR, Bakker BM, Matthews K and Clayton C: Transcriptome-wide analysis of mRNA decay reveals complex degradation kinetics and suggests a role for co-transcriptional degradation in determining mRNA levels. *Mol Microbiol* 2014; 94, 307-26. 10.1111/mmi.12764

Begolo D., Erben E. and Clayton C: Drug target identification using a trypanosome over-expression library. *Antimicrob Agents Chemother* 2014; 58, 6260-4. 10.1128/AAC.03338-14

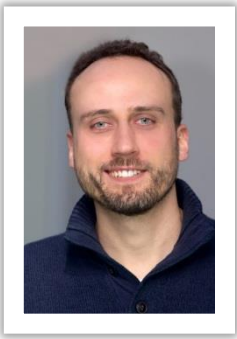
Erben E, Fadda A, Lueong S, Hoheisel JD and Clayton C: Genome-wide discovery of post-transcriptional regulators in *Trypanosoma brucei*. *PLoS Pathogens* 2014; 10, e1004178. doi:10.1371/journal.ppat.1004178

Singh A, Minia I, Droll D, Fadda A, Clayton C, Erben E: Trypanosome MKT1 and the RNA-binding protein ZC3H11: interactions and potential roles in post-transcriptional regulatory networks. *Nucleic Acids Res* 2014; 42, 4652-68; 10.1093/nar/gkt1416

Clayton C: The regulation of trypanosome gene expression by RNA-binding proteins. *PLoS Pathogens* 2013, 10.1371/journal.ppat.1003680 Review

Droll D, Minia I, Fadda A, Singh A, Stewart M, Queiroz R, Clayton C: Post-transcriptional regulation of the trypanosome heat shock response by a zinc finger protein. *PLoS Pathogens* 2013; 9, e1003286, doi:10.1371/journal.ppat.1003286

List of the Associated Research Groups Major Infectious Diseases



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Specific Research Interests

- Cell intrinsic immune defense and inflammatory signaling pathways
- Regulation and dynamics of signaling events
- Dynamics of RNA-virus replication
- Virus-host interactions in innate immunity
- Systems biology and mathematical modeling



apl. PD Dr. Martin Müller

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Specific Research Interests

- Prophylactic and therapeutic vaccination against human papillomaviruses (HPV)
- Scaffolds for vaccine antigens
- Natural and vaccine induced immunity against HPV
- Host cell restriction and dependency factors for adeno-associated viruses (AAV) and HP



Dr. Ellen Krautkrämer

Research Group "*Hantavirus pathogenesis*"
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Specific Research Interests

- replication cycle of hantaviruses in renal cells
- clinical characteristics of hantavirus infection
- mechanisms of hantavirus-induced cellular damage and renal failure



PD Dr. Dr. Angelika Riemer

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Specific Research Interests

- Therapeutic cancer vaccines, especially against HPV-mediated malignancies
- Direct (MS-based) detection of CTL target epitopes on the surface of infected or transformed cells
- Therapeutic vaccine design and formulation
- Directing vaccination-induced T cells to certain body sites
- HPV-induced changes in antigen processing and presentation



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Specific Research Interests

- Spuma Retroviruses (Foamy Viruses)
- Vaccine vector development
- Virus-host interaction in virus replication in vitro and in vivo
- Retrovirus assembly, morphogenesis and release
- APOBEC₃ proteins: antiviral restriction factors and cancer genome mutators



Prof. Dr. R. Luise Krauth-Siegel

Research Group "Trypanosomes and drug design"
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Specific Research Interests

- Trypanothione metabolism of trypanosomes
- Antioxidant defense mechanisms
- Parasite specific enzymes as drug target molecules



Prof. Dr. Hedda Wardemann

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Specific Research Interests

- Human immune responses against *Plasmodium falciparum*
- Malaria vaccine development
- Immunological memory to infection and vaccination
- Antigen-receptor diversity and quality of immune responses



Dr. Erec Stebbins

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Specific Research Interests

- Microbial pathogens as they relate to immunology and human carcinogenesis
- Structural biology/X-ray crystallography
- The African trypanosome (*T. brucei*), the causative agent of sleeping sickness
- Genotoxins or agents impacting oncogenic growth regulatory factors in the cell



Prof. Dr. F. Nina Papavasiliou

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Specific Research Interests

- Surface receptor diversification in the African trypanosome (*T. brucei*), the causative agent of sleeping sickness
- The interface between host immunity (antibodies) and the ever changing coat composition of *T. brucei* (also known as antigenic variation)
- Informational diversity through epitranscriptomic mechanisms in host immune cells.

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Students of the “Major Infectious Diseases” WS2016-2017



From left to right, in the back: Yannik Voß, Léanne Strauß, Jasmin Dehnen, Tammy Lan, Christian Sommerauer, Moritz König. In the middle: Micha Rosenkranz, Thomas Kehrer, Emma Pietsch, Franziska Kraus, Benjamin Lang, Silke Schmidt, Anna Huhn. In the front: Sabina Ganskih, Julia Heinze.