



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, SARS 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/zentrum-fuer-infektiologie/zentrum-fuer-infektiologie>). 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 are further strengthened by the new CIID building (INF 344) opened in November 2017, which houses many

groups from the Department of Infectious Diseases and offers state of the art equipment, in particular an Infectious Disease Imaging Platform

(<https://www.idip-heidelberg.org/>) for imaging of pathogens by a broad spectrum of advanced methods.

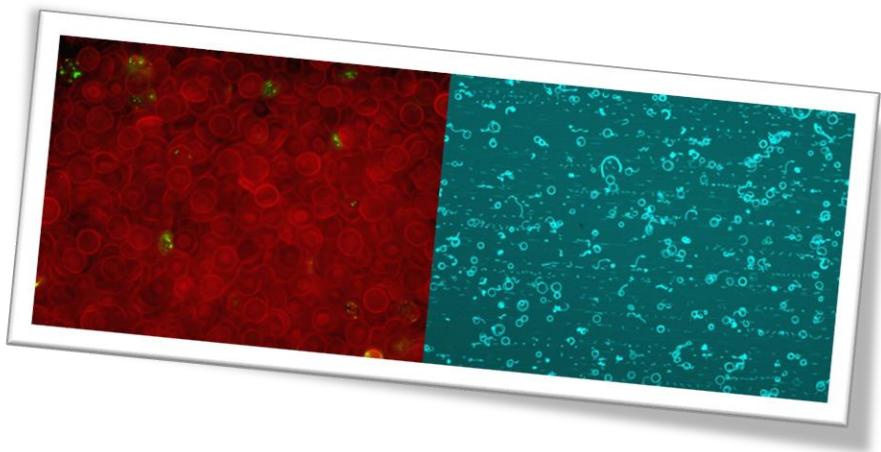
Beyond that, all research groups of the department are connected within local and international research consortia and networks, some of which are coordinated by members of the department. This comprises the Cluster of Excellence "CellNetworks" (<http://www.cellnetworks.uni-hd.de/>), the German Center for Infection Research "DZIF" (<http://www.dzif.de/>) as well as DFG collaborative research centers: SFB1129 (<http://www.sfb1129.de/>), TRR179 (<http://www.trr179.de/>), TRR83 (<http://www.trr83.de/>), TRR319 (<https://rmap.uni-mainz.de/>), TRR186 (<https://trr186.uni-heidelberg.de/>) and the DFG priority program 1923 (<https://spp1923.de/>).

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 and the associated research groups participating in this Major can be found in the profiles provided below 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".



courses on microbiology, infectious disease immunology, parasitology and virology in Semesters 4 and 5.

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 interested in this Major are advised to attend the lectures and

## Acquired Degree

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

Various doctoral study programs are offered by the institutes involved in the "Infectious Diseases" Major. Further information is to be found on the websites of the participating departments.

### CONTACT POINT

Major Infectious Diseases

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Internet:

<https://www.klinikum.uni-heidelberg.de/zentrum-fuer-infektiologie/molecular-virology/major-infectious-diseases>



## 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:

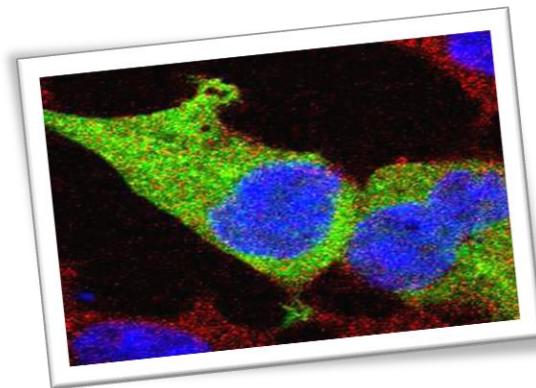
- Medical Microbiology and Hygiene
- Molecular Virology
- Virology
- Integrative Virology
- Parasitology

# 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. med. Alexander Dalpke (Head of the Medical Microbiology)
- apl. Prof. Dr. Katharina Hieke-Kubatzky

## Prof. Dr. Alexander Dalpke



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## Scientific Vita

Since 2022: Full Professor (W3) for Medical Microbiology and Hygiene, Medical Director, Medical Microbiology and Hygiene, Dept. of Infectious Diseases, University Hospital Heidelberg

2019-2022: Full Professor (W3) for Medical Microbiology; Medical Director, Institute of Medical Microbiology and Virology; Medical Faculty, Technical University Dresden

2013-2018: Deputy Medical Director, Medical Microbiology and Hygiene, Dept. of Infectious Diseases, Heidelberg University

2011: Consultant Microbiologist

2006: Consultant Immunologist (DGfI)

2006-2018: Professor (W3) for Medical Microbiology and Infection and Immunity, Dept. of Medical Microbiology and Hygiene, University Heidelberg

Since 2005: Independent Group Leader, Dept. of Hygiene and Med. Microbiology, Heidelberg

2004: Venia legendi, Habilitation; University lecturer for infection and immunity, Med. Faculty, Philipps-University Marburg

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

1999: License to practice medicine

1998: MD in Medical Microbiology, University Göttingen (summa cum laude)

1992-1998: Human Medicine, University Göttingen

## Specific Research Interests

- Immunostimulation by nucleic acids
- Microbiome analysis in cystic fibrosis

## Selected Publications

Kolbe U, Yi B, Poth T, Saunders A, Boutin S and Dalpke A: Early cytokine induction upon *Pseudomonas aeruginosa* infection in murine precision cut lung slices depends on sensing of bacterial viability. *Front Immunol* 2020; 11: 598636

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; 50(4): 1701086

Eigenbrod T, Pelka K, Latz E, Kreikemeyer B and Dalpke AH: TLR8 Senses Bacterial RNA in Human Monocytes and Plays a Nonredundant Role for Recognition of *Streptococcus pyogenes*. *J Immunol* 2015; 195(3): 1092-1099

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 and 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 NF $\kappa$ B signaling by decreasing p65 stability within the cell nucleus. *FASEB J* 2011; 25(3): 863-874

Schmidt LM, Belvisi MG, Bode KA, Bauer J, Schmidt C, Suchy MT, Tsikas D, Scheuerer J, Lasitschka F, Gröne HJ and Dalpke AH: Bronchial epithelial cell-derived prostaglandin E2 dampens the reactivity of dendritic cells. *J Immunol.* 2011; 186(4): 2095-2105

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

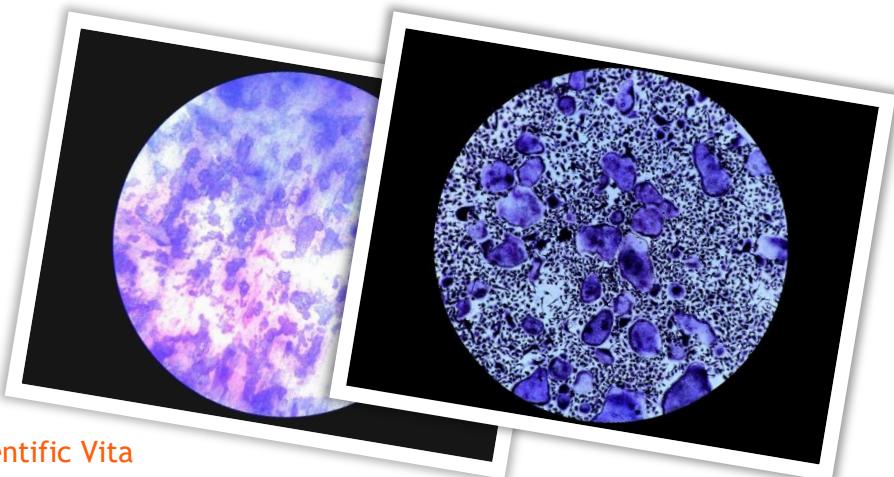
Bätz A, Frey M, Heeg K and Dalpke AH: Suppressor of cytokine signaling (SOCS) proteins indirectly regulate Toll-like receptor signaling in innate immune cells. *J Biol Chem* 2004; 279(52): 54708-54715

## apl. Prof. Dr. Katharina Hieke-Kubatzky



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## Scientific Vita

2018: Professorship (apl.) at Heidelberg University

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

- Osteoimmunology: interactions between bone and immune cells
- Immune-metabolism and osteoclast differentiation: We investigate the ability of metabolic enzymes to modulate the plasticity of macrophages and their ability to become osteoclasts
- Staphylococci in bone infection: we aim to understand the crosstalk between bacteria and immune cells/osteoclasts
- Plumbagin-mediated effects on bone cells: This phytochemical is a potent ROS inducer with (anti)osteoclastic properties

## Selected Publications

Sultanli S, Ghumnani S, Ashma R, Kubatzky KF: Plumbagin, a Biomolecule with (Anti)Osteoclastic Properties. *Int J Mol Sci* 2021; 22(5):2779

Lemke C, Benýšek J, Brajtenbach D, Breuer C, Jílková A, Horn M, Buša M, Ulrychová L, Illies A, Kubatzky KF, Bartz U, Mareš M, Gütschow M: An Activity-Based Probe for Cathepsin K Imaging with Excellent Potency and Selectivity. *J Med Chem* 2021; 64(18):13793-13806

Seebach E, Kubatzky KF: Chronic Implant-Related Bone Infections-Can Immune Modulation be a Therapeutic Strategy? *Front Immunol* 2019; 10:1724

Nair A, Chauhan P, Saha B, Kubatzky KF: Conceptual Evolution of Cell Signaling. *Int J Mol Sci* 2019; 20(13):3292

Kubatzky KF, Uhle F, Eigenbrod T: From macrophage to osteoclast - How metabolism determines function and activity. *Cytokine*. 2018; 112:102-115

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

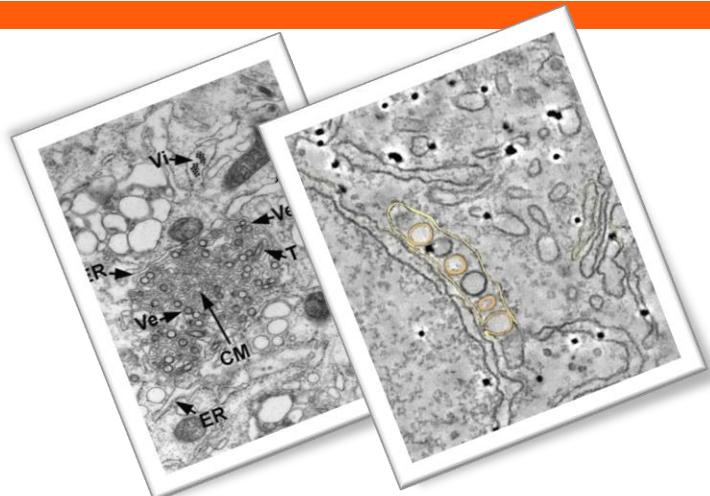
Hildebrand D, Bode KA, Rieß D, Cerny D, Waldhuber A, Römmler F, Strack J, Korten S, Orth JH, Miethke T, Heeg K, Kubatzky KF: Granzyme A produces bioactive IL-1 $\beta$  through a non-apoptotic inflammasome-independent pathway. *Cell Rep* 2014; 6:9(3): 910-7

# 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), hepatitis D virus (HDV) and several flaviviruses, most notably Dengue virus (DENV), Zikavirus (ZIKV) and, most recently, coronaviruses such as SARS-CoV-2. These viruses are leading causes for death worldwide with about 400 million people suffering from a chronic infection with HBV/HDV 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 and development of viral diagnostics and antiviral drugs. 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 (DZIF Professorship for Translational Virology)
- apl. Prof. Dr. Volker Lohmann (Head of Section „Virus Host Interactions“)
- Dr. Alessia Ruggieri

## Prof. Dr. Dr. h.c. Ralf Bartenschlager



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Web: www.molecular-virology.uni-hd.de

## 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, ZIKV and SARS-CoV-2)
- Structural and functional aspects of viral RNA replication and assembly
- Viral and host targets for antiviral therapy
- Innate immune responses and viral countermeasures
- Strategies of viral persistence



## Selected Publications

Ke Z, Oton J, Qu K, Cortese M, Zila V, McKeane L, Nakane T, Zivanov J, Neufeldt CJ, Cerikan B, Lu JM, Peukes J, Xiong X, Kräusslich HG, Scheres SHW, Bartenschlager R, Briggs JAG: Structures and distributions of SARS-CoV-2 spike proteins on intact virions. *Nature* 2020; doi: 10.1038/s41586-020-2665-2 Epub ahead of print. PMID: 32805734

Neufeldt CJ, Cortese M, Scaturro P, Cerikan B, Wideman JG, Tabata K, Moraes T, Oleksiuk O, Pichlmair A, Bartenschlager R: ER-shaping atlasin proteins act as central hubs to promote flavivirus replication and virion assembly. *Nat Microbiol.* 2019; (12):2416-2429

Lauber C, Seitz S, Mattei S, Suh A, Beck J, Herstein J, Bördold J, Salzburger W, Kaderali L, Briggs JAG, Bartenschlager R: Deciphering the Origin and Evolution of Hepatitis B Viruses by Means of a Family of Non-enveloped Fish Viruses. *Cell Host Microbe* 2017; 22(3):387-399

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

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)

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, Tschoop 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

## Prof. Dr. Stephan Urban



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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: CHS 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 (bulivertide) for HBV/HDV infection
- Development of hepatotropic drugs for the therapy of liver diseases
- Development of point of care (POC) test for HDV

## Selected Publications

Wedemeyer H, Schönweis K, et al and Urban S: A multicentre, randomised, parallel-group, open-label phase 2 clinical trial (MYR202) to assess safety and efficacy of bolevirtide in combination with tenofovir disoproxil fumarate in patients with HBV/HDV coinfection. *Lancet Infect Dis* 2022; in press

Zhang Z, Ni Y, Lempp FA, Walter L, Mutz P, Bartenschlager R and Urban S: Hepatitis D virus-induced interferon response and administered interferons control cell division-mediated virus spread. *J Hepatol* 2022; 168-8278(22)00338-5

Urban S, Neumann-Haefelin C and Lampertico P: Hepatitis D virus in 2021: virology, immunology and new treatment approaches for a difficult-to-treat disease. *Gut* 2021; 70(9):1782-1794

Tu T, Zehnder B, Qu B and Urban S: De novo synthesis of Hepatitis B virus nucleocapsids is dispensable for the maintenance and transcriptional regulation of cccDNA. *JHEP Rep* 2020; 3(1):100195

Lempp FA, Schlund F, Rieble L, Nussbaum L, Link C, Zhang Z, Ni Y, Urban S: Recapitulation of HDV infection in a fully permissive hepatoma cell line allows efficient drug evaluation. *Nat Commun.* 2019; 10.1038/s41467-019-10211-2

Zhang Z, Filzmayr C, Ni Y, Sültmann H, Mutz P, Hiet MS, Vonrnan FWR, Bartenschlager R, Urban S: Hepatitis D virus replication is sensed by MDA5 and induces IFN-β/λ responses in hepatocytes. *J Hepatol* 2018; 69(1):25-35

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

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

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

Gripion 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

## apl. Prof. Dr. Volker Lohmann



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Web: www.molecular-virology.uni-hd.de

### Scientific Vita

2020: Head of Section „Virus Host Interactions“

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
- Function of norovirus nonstructural proteins

### Selected Publications

Heuss C, Rothhaar P, Burm R, Lee JY, Ralfs P, Haselmann U, Ströh LJ, Colasanti O, Tran CS, Schäfer N, Schnitzler P, Merle U, Bartenschlager R, Patel AH, Graw F, Krey T, Laketa V, Meuleman P and Lohmann V: A Hepatitis C virus genotype 1b post-transplant isolate with high replication efficiency in cell culture and its adaptation to infectious virus production in vitro and in vivo. *PLoS Pathog* 2022; 18(6):e1010472

Grünvogel O, Colasanti O, Lee JY, Klöss V, Belouzard S, Reustle A, Esser-Nobis K, Hesebeck-Brinckmann J, Mutz P, Hoffmann K, Mehrabi A, Koschny R, Vondran FWR, Gotthardt D, Schnitzler P, Neumann-Haefelin C, Thimme R, Binder M, Bartenschlager R, Dubuisson J, Dalpke AH, Lohmann V: Secretion of Hepatitis C Virus Replication Intermediates Reduces Activation of Toll-Like Receptor 3 in Hepatocytes. *Gastroenterology* 2018; 154(8):2237-2251

Schult P, Roth H, Adams RL, Mas C, Imbert L, Orlik C, Ruggieri A, Pyle AM, Lohmann V: microRNA-122 amplifies hepatitis C virus translation by shaping the structure of the internal ribosomal entry site. *Nat Commun* 2018; 9(1):2613

Doerflinger SY, Cortese M, Romero-Brey I, Menne Z, Tubiana T, Schenk C, White PA, Bartenschlager R, Bressanelli S, Hansman GS, Lohmann V: Membrane alterations induced by nonstructural proteins of human norovirus. *PLoS Pathog* 2017; 27(13):e101238

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Harak C, Meyrath M, Romero-Brey I, Schenk C, Gondeva 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, Francescu 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.

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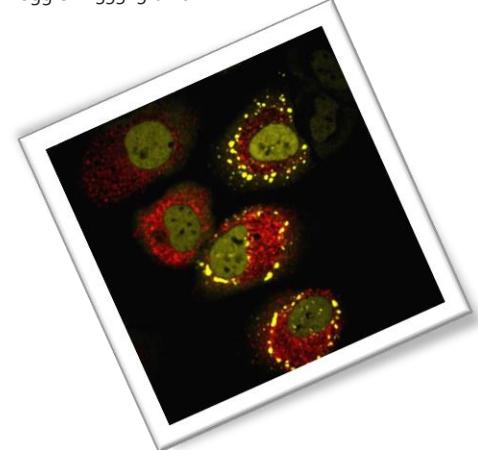
Lohmann V., Körner F., Koch JO, Herian U, Theilmann L and Bartenschlager R.: Replication of subgenomic hepatitis C virus RNAs in a hepatoma cell line. *Science* 1999; 285: 110-113

## Dr. Alessia Ruggieri



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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

2004–2008: PostDoc at the Institute of Human Genetics, University of Saarland

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
- Crosstalk between host stress and innate immune responses
- Interplay of Flaviviruses with the host cell translation machinery
- Unconventional translation initiation of dengue virus genome
- Flavivirus epitranscriptomics: role of RNA modifications in the flavivirus life cycle

## Selected Publications

Klein P\*, Kallenberger SM\*, Roth H, Roth K, Ly-Hartig TBN, Magg V, Aleš J, Talemi SR, Qiang Y, Wolf S, Oleksiuk O, Kurilov R, Di Ventura B, Bartenschlager R, Eils R, Rohr K, Hamprecht FA, Höfer T, Fackler OT,

Stoecklin G, Ruggieri A: Temporal control of the integrated stress response by a stochastic molecular switch. *Science Advances* 2022; 8(12):eabk2022

Ruggieri A, Helm M, Chatel-Chaix L: An epigenetic "extreme makeover": the methylation of flaviviral RNA (and beyond). *RNA Biology* 2021; 18:1-13

Eiermann N, Haneke K, Sun Z, Stoecklin G, Ruggieri A: Dance with the devil: Stress granules and signaling in antiviral responses. *Viruses* 2020; 12(9), 984

Haneke K, Schott J, Lindner D, Hollensen AK, Damgaard CK, Mongis C, Knop M, Palm W, Ruggieri A, Stoecklin G: CDK1 couples proliferation with protein synthesis. *J Cell Biol.* 2020; 219(3): e201906147

Brocard M, Iadevaia V, Klein P, Hall B, Lewis G, Lu J, Burke J, Willcocks M, Parker R, Goodfellow IG, Ruggieri A, Locker N: Norovirus infection results in eIF2 $\alpha$ -independent host translation shut-off and remodels

the G3BP1 interactome evading stress granule formation. *PLoS Pathog.* 2020; 16(1):e1008250

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(1):e02150-16

Brocard M, Ruggieri A, Locker N: m6A RNA methylation, a new hallmark in virus-host interactions. *J Gen Virol.* 2017; 98(9):2207-2214

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.

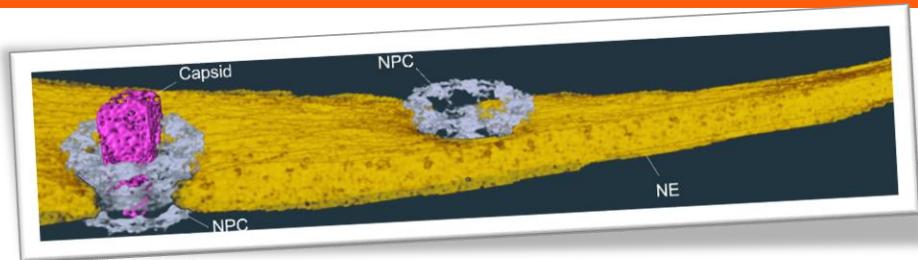
# Virology

## Fields of Interest

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

A major focus of our research is human immunodeficiency virus (HIV), the causative agent of AIDS (Kräusslich, Müller). In spite of 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.

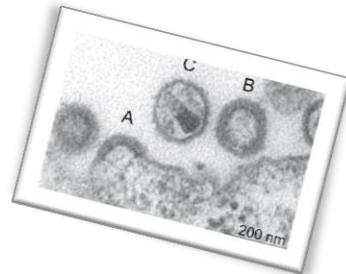
Other viral systems studied include parvoviruses, the enteropathogens norovirus and reovirus, bunyaviruses, influenza virus and hepatitis E virus. We develop and use vectors based on adeno-associated virus for basic research and gene therapy approaches (Grimm) and exploit the CRISPR/Cas system for gene 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, and the group of Dao Thi studies interactions between Hepatitis E virus and host cells in stem-cell derived culture systems. Finally, we are interested in influenza virus structure, particle formation and entry, and in the role of host proteins and lipids in these processes (Kräusslich, Chlanda). Combination of conventional virological approaches with a wide variety of specialized techniques (e.g. cryo-electron tomography, high throughput approaches, advanced fluorescence microscopy techniques, x-ray crystallography and more) is employed to address our virological questions.

The following teams belong to the Virology:

- Prof. Dr. Hans-Georg Kräusslich (Head of the Virology)
- Prof. Dr. Dirk Grimm
- apl. Prof. Dr. Barbara Müller
- Dr. Frauke Mücksch
- Dr. Petr Chlanda
- Dr. Viet Loan Dao Thi



### Prof. Dr. Hans-Georg Kräusslich



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Web: <http://www.klinikum.uni-heidelberg.de/index.php?id=6550&L=1>

#### Scientific Vita

2019–present: Dean of the Medical Faculty, Heidelberg University

2019–2021: coordinator, German Center of Infectious Disease Research

2014–2019: 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, Leibniz Institute of Virology, Hamburg

1996–1999: Director, Leibniz Institute of Virology, 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)

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## Specific Research Interests

- Cell biology of virus infection
- Virus-host interactions in the early post-entry phase of viral replication
- Nuclear import of HIV-1
- Structural and functional analyses of HIV-1 and influenza virus assembly and release
- HIV Protease and antiviral resistance

## Selected Publications

Müller TG, Zila V, Müller B, Kräusslich HG: Nuclear Capsid Uncoating and Reverse Transcription of HIV-1. *Annual review of virology* 2022

Qu K, Ke Z, Zila V, Anders-Össwein M., Glass B, Mücksch F, Müller R, Schultz C, Müller B, Kräusslich HG, Briggs JAG: Maturation of the matrix and viral membrane of HIV-1. *Science* 2021; 373, 700-704

Zila, V., Margiotta, E., Turonova, B., Müller, T.G., Zimmerli, C.E., Mattei, S., Allegretti, M., Borner, K., Rada, J., Müller, B., et al.: Cone-shaped HIV-1 capsids are transported through intact nuclear pores. *Cell* 2021; 184, 1032-1046 e1018

Müller TG, Zila, V., Peters K, Schifferdecker S, Stanic M, Lucic B, Laketa V, Lusic M, Müller B, Kräusslich HG: HIV-1 uncoating by release of viral cDNA from capsid-like structures in the nucleus of infected cells. *eLife* 2021; doi: 10.7554/eLife.64776

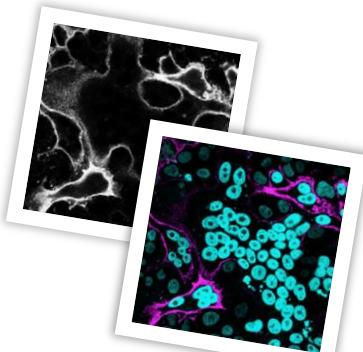
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Mücksch F, Laketa V, Müller B, Schultz C, Kräusslich HG: Synchronized HIV assembly by tunable PIP<sub>2</sub> changes reveals PIP<sub>2</sub> requirement for stable Gag anchoring. *eLife* 2017; pii: e25287. doi: 10.7554/eLife.25287

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; 10(9):8215-22

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



## apl. Prof. Dr. Barbara Müller



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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, Leibniz Institute of Virology, 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>

Schifferdecker S, Zila V, Müller TG, Sakin V, Anders-Össwein M, Laketa V, Kräusslich HG, Müller B: Direct Capsid Labeling of Infectious HIV-1 by Genetic Code Expansion Allows Detection of Largely Complete Nuclear Capsids and Suggests Nuclear Entry of HIV-1 Complexes via Common Routes. *MBio* 2022; doi: 10.1128/mbio.01959-22

Müller TG, Zila V, Müller B, Kräusslich HG: Nuclear Capsid Uncoating and Reverse Transcription of HIV-1. *Annual review of virology* 2022

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Zila V, Margiotta E, Turonova B, Müller TG, Zimmerli CE, Mattei S, Allegretti M, Borner K, Rada J, Müller B, et al.: Cone-shaped HIV-1 capsids are transported through intact nuclear pores. *Cell* 2021; 184, 1032-1046 e1018

Müller TG, Zila, V., Peters K, Schifferdecker S, Stanic M, Lucic B, Laketa V, Lusic M, Müller B, Kräusslich HG: HIV-1 uncoating by release of viral cDNA from capsid-like structures in the nucleus of infected cells. *eLife* 2021; doi: 10.7554/eLife.64776

Pape C, Remme R, Wolny A, Olberg S, Wolf S, Cerrone L, Cortese M, Klaus S, Lucic M, Ullrich S, Wolf S, Cerikan B, Neufeldt CJ, Ganter M, Schnitzler P, Merle U, Lusic M, Boulant S, Stanifer M, Bartenschlager R, Hamprecht FA, Kreshuk A, Tischer C, Kräusslich HG, Müller B, Laketa V: Microscopy-based assay for semi-quantitative detection of SARS-CoV-2 specific antibodies in human sera: A semi-quantitative, high throughput, microscopy-based assay expands existing approaches to measure SARS-CoV-2 specific antibody levels in human sera. *BioEssays* 2021; 43, e2000257

Müller TG, Sakin V, Müller B: A Spotlight on Viruses—Application of Click Chemistry to Visualize Virus-Cell Interactions. *Molecules* 2019; doi: 10.3390/molecules24030481

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

Schimer J, Pavova M, Anders M, Pachl 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 photodestructible protease inhibitor. *Nature Communications* 2015; 6:6461

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

## Prof. Dr. Dirk Grimm



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Web: <https://grimm-labs.com/>

### Scientific Vita

2022-present: Full professor (W3) "Virale Vektortechnologie" at the Medical Faculty of the Heidelberg University Hospital

2017-2022: Professor (W2) "Virale Vektortechnologie", at the Medical Faculty of the Heidelberg University Hospital

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

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

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

1999-2001: PostDoc, 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 parasitic 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

Andari JE, Renaud-Gabardos E, Tulalamba W, Weinmann J, Mangin L, Pham QH, Hille S, Bennett A, Attebi E, Bourges E, Leborgne C, Guerchet N, Fakhiri J, Krämer C, Wiedtke E, McKenna R, Guianvarc'h L, Toueille M, Ronzitti G, Hebben M, Mingozzi F, VandenDriessche T, Agbandje-McKenna M, Müller OJ, Chuah MK, Buj-Bello A, Grimm D: Semi-rational bioengineering of AAV vectors with increased potency and specificity for systemic gene therapy of muscle disorders. *Sci Adv* 2022; in press.

Weinmann J, Weis S, Sippel J, Tulalamba JW, Remes A, El Andari J, Herrmann AK, Pham QH, Borowski C, Hille S, Schöneberger T, Frey N, Lenter M, VandenDriessche T, Müller OJ, Chuah MK, Lamla T, Grimm D: Identification of a myotropic AAV by massively parallel in vivo evaluation of barcoded capsid variants. *Nat Commun* 2020; 28: 5432

Börner K, Kienle E, Huang LY, Weinmann J, Sacher A, Bayer P, Stöllein C, Fakhiri J, Zim-mermann L, Westhaus A, Beneke J, Beil N, Wiedtke E, Schmelas C, Miltner D, Rau A, Erfle H, Kräusslich HG, Müller M, Agbandje-McKenna M, Grimm D: Pre-arrayed pan-AAV peptide display libraries for rapid single-round screening. *Mol Ther* 2020; 28:1016-1032

Senís E, Mosteiro L, Wilkening S, Wiedtke E, Nowrouzi A, Afzal S, Fronza R, Landerer H, Abad M, Niopék D, Schmidt M, Serrano M, Grimm D: AAV vector-mediated in vivo reprogramming into pluripotency. *Nat Commun* 2018; 9:2651

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

Rezvani M, Espanol-Suner R, Malato Y, Dumont L, Grimm AA, Kienle E, Bindman J, Wiedtke E, Hsu BY, Naqvi SJ, Schwabe RF, Covera CU, Grimm D, Willenbring H: In vivo reprogramming of myofibroblasts into hepatocytes as a therapeutic strategy for liver fibrosis. *Cell Stem Cell* 2016; 18:809-816

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

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

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

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

## Dr. Viet Loan Dao Thi



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### Scientific Vita

2018-present: Chica and Heinz Schaller Junior Group Leader, University Hospital Heidelberg

2015-2017: Postdoctoral fellow, The Rockefeller University, USA

2012-2014: Postdoctoral associate, Institute of Microbiology of the University Hospital Centre Vaudois and of the University of Lausanne, Switzerland

2007-2011: PhD, Ecole Normale Supérieure de Lyon, France

2003-2004: MSc, Dongseo University, South Korea

2000-2006: Dipl.-Ing, Berlin Institute of Technology, Germany

### Specific Research Interests

- Molecular virology, virus-host interaction, virus life cycle
- Hepatotropic viruses with a special focus on hepatitis E virus (HEV)
- Stem cell technology for improved cell culture models
- Personalized models of virus infection, precision medicine
- Antiviral therapy and therapy resistance

### Selected Publications

Maurer L, El Andari J, Rapti K, Spreyer L, Steinmann E, Grimm D, Dao Thi VL: Induction of Hepatitis E virus anti-ORF3 antibodies from systemic administration of a muscle-specific adeno-associated virus (AAV) vector. *Viruses* 2022; 14(2): 266

Zhang C, Freistaedter A, Schmelas C, Gunkel M, Dao Thi VL, Grimm D: An RNA interference/adeno-associated virus vector-based combinatorial gene

therapy approach against Hepatitis E virus. *Hepatol Commun.* 2021; 6(4):878-888

Bove G, Mehnert A-K, Dao Thi VL: Chapter 7, iPSCs for modeling hepatotropic pathogen infections, Editor: Alexander Birbrair, In Advances in Stem Cell Biology, iPSCs for Studying Infectious Diseases, Academic Press 2021; Volume 8, p. 149-213

Dao Thi VL, Wu X, Belote RL, Andreo U, Takacs CN, Fernandez JP, Vale-Silva LA, Decker CC, Fu RM, Qu B, Uryu K, Molina H, Saeed M, Steinmann E, Urban S, Singaraja RR, Schneider WM, Simon SM, Rice CM: Stem cell-derived polarized hepatocytes. *Nature Commun.* 2020; 11(1):1677

Fu RM, Decker CC, Dao Thi VL: Cell Culture Models for Hepatitis E Virus. *Viruses* 2019; 11(7):608

Wu X, Dao Thi VL, Liu P, Takacs CN, Xiang K, Andrus L, Gouttenoire J, Moradpour D, Rice CM: Pan-Genotype Hepatitis E Virus Replication in Stem Cell-Derived Hepatocellular Systems. *Gastroenterology* 2018; 154(3):663-674

Wu X, Dao Thi VL, Huang Y, Billerbeck E, Saha D, Hoffmann HH, Wang Y, Vale Silva LA, Sarbanes S, Sun T, Andrus L, Quirk C, MacDonald MR, Schneider WM, An X, Rosenberg BR, Rice CM: Intrinsic Immunity Shapes Viral Resistance of Stem Cells. *Cell* 2018; 172(3):423-438

Dao Thi VL, Debing Y, Wu X, Rice CM, Neyts J, Moradpour D, Gouttenoire J: Sofosbuvir inhibits Hepatitis E virus replication in vitro and results in an additive effect when combined with ribavirin. *Gastroenterology* 2016; 150:82-85

## Scientific Vita

2017-present: Schaller research group leader at the Department for Infectious Diseases-Virology, University of Heidelberg Medical School

2011-2017: Postdoc at the National Institutes of Health, Bethesda, USA

2010-2011: Postdoc at the European Molecular Biology Laboratory, Heidelberg, Germany

2006-2010: Ph.D. at Heidelberg University, Heidelberg, Germany

2000-2006: M.S. at Charles University, Prague, Czech Republic

## Specific Research Interests

- virology
- cryo-electron microscopy
- membranes and lipids
- cell biology
- membrane fusion

## Selected Publications

Chlanda P, Mekhedov E, Waters H, Sodt A, Schwartz C, Nair V, Blank PS, Zimmerberg J: Palmitoylation contributes to membrane curvature in Influenza A virus assembly and hemagglutinin-mediated membrane fusion. *J Virol* 2017; 91(21)

Chlanda P: Influenza Hemagglutinin and M<sub>2</sub> ion channel priming by trypsin: Killing two birds with one stone. *Virology* 2017; 509:131-132

Chlanda P, Krijnse Locker J: The sleeping beauty kissed awake: new methods in electron microscopy to study cellular membranes. *Biochem J* 2017; 474(6):1041-1053

Quemin ERJ, Chlanda P, Sachse M, Forterre P, Prangishvili D, Krupovic M: Eukaryotic-like virus budding in Archaea. *MBio* 2016; 13(7)(5)

Chlanda P, Mekhedov E, Waters H, Schwartz CL, Fischer ER, Ryham RR, Cohen FS, Blank PS, Zimmerberg J: The hemifusion structure induced by Influenza virus hemagglutinin is determined by physical properties of the target membranes. *Nat Microbiol* 2016; 18(16):16050

Chlanda P, Zimmerberg J: Protein-lipid interactions critical to replication of the influenza A virus during infection. *FEBS Lett* 2016; 590(13):1940-54

Chlanda P, Schraadt O, Kummer S, Riches J, Oberwinkler H, Prinz S, Kräusslich HG, Briggs JAG: Structural analysis of the contributions of individual proteins to influenza assembly and morphology. *J Virol* 2015; 89(17):8957-66

Chlanda P, Sachse M: Cryo-Electron Microscopy of Vitreous Sections. *Methods Mol Biol* 2014; 1117:193-214

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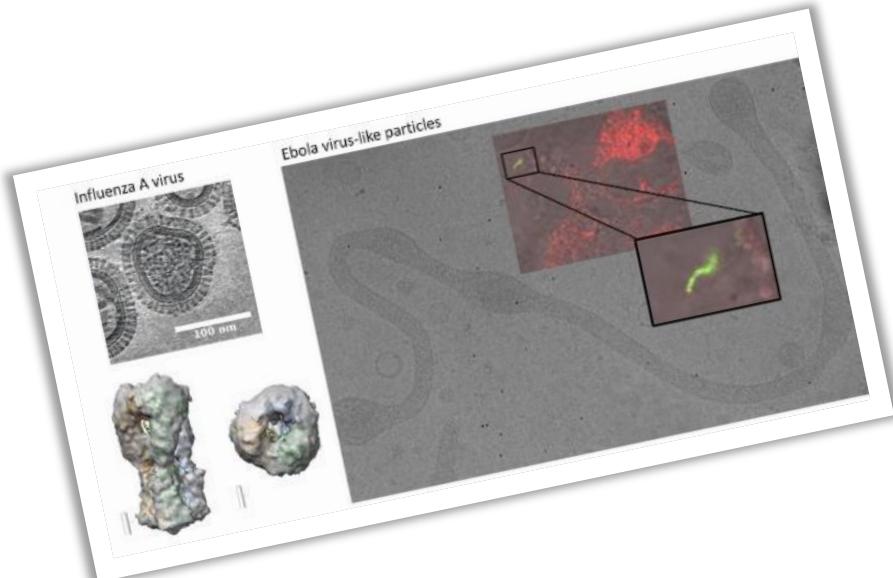
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## Dr. Frauke Mücksch



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Web: <https://www.klinikum.uni-heidelberg.de/zentrum-fuer-infektiologie/virologie/forschung/forschungsgruppen/muecksch>

## Scientific Vita

2022-present: Chica and Heinz Schaller Junior Group Leader, Department of Infectious Diseases, Virology, Heidelberg University

2019-2022: PostDoc, The Rockefeller University, New York, USA

2018-2019: PostDoc, Department of Infectious Diseases, Heidelberg University

2013-2017: PhD in virology with Summa cum laude, Heidelberg University

2011-2013: MSc (Biomedical Science), University of Marburg

2008-2011: BSc (Biology), University of Frankfurt

## Specific Research Interests

- Molecular virology, virus-host interaction
- Immuno- and cell biology of HIV-1 infection
- Regulation of HIV-1 transcription
- Establishment and reversal of HIV-1 latency

## Selected Publications

Muecksch F\*, Wise H\*, Templeton K, Batchelor B, Squires M, McCance K, Jarvis L, Malloy K, Furrie E, Richardson C, MacGuire J, Goldberl, Burns A, Marvin A, Zhang F, Schmidt F, Bieniasz PD, Jenks S, Hatzioannou T: Longitudinal variation in SARS-CoV-2 antibody levels and emergence of SARS-CoV-2 variants: a serological analysis. *Lancet Microbe* 2022; 3(7):e493-502

Muecksch F\*, Wang Z\*, Cho A\*, Gaebler C, Ben Tanfous T, DaSilva J, Bednarski E, Ramos V, Zong S, Johnson B, Raspe R, Schaefer-Babajew D, Shimeliovich I, Daga M, Yao K-H, Schmidt F, Millard KG, Turroja M, Jankovic M, Oliviera TY, Gazumyan A, Caskey M, Hatzioannou T, Bieniasz PD, Nussenzweig MC: Increased memory B cell potency and breadth after a SARS-CoV-2 mRNA boost. *Nature* 2022; 607(7917):128-134

Cho A\*, Muecksch F\*, Schaefer-Babajew\* D, Wang Z\*, Finkin S\*, Gaebler C, Ramos V, Cipolla M, Mendoza P, Agudelo M, Bednarski E, DaSilva E, Shimeliovich I, Dizon J, Daga M, Millard K, Turroja M, Schmidt F, Zhang F, Tanfous TB, Jankovic M, Oliveira TY, Gazumyan A, Caskey M, Bieniasz PD, Hatzioannou T, Nussenzweig MC: Anti-SARS-CoV-2 receptor binding domain antibody evolution after mRNA vaccination. *Nature* 2021; 600(7889):517-522 \*co-first author

Muecksch F\*, Weisblum Y\*, Barnes CO\*, Schmidt F\*, Schaefer-Babajew D, Wang Z, C Lorenzi JC, Flyak AI, DeLaitch AT, Huey-Tubman KE, Hou S, Schiffer CA, Gaebler C, Da Silva J, Poston D, Finkin S, Cho A, Cipolla M, Oliveira TY, Millard KG, Ramos V, Gazumyan A, Rutowska M, Caskey M, Nussenzweig MC, Bjorkman PJ, Hatzioannou T, Bieniasz PD: Affinity maturation of SARS-CoV-2 neutralizing antibodies confers potency, breadth, and resilience to viral escape mutations. *Immunity* 2021; 54, 1853-1868

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Silva J, Bednarski E, Aguado L, Yee J, Daga M, Turroja M, Millard KG, Jankovic M, Gazumyan A, Zhao Z, Rice CM, Bieniasz PD, Caskey M, Hatzioannou T, Nussenzweig MC: Naturally enhanced neutralizing breadth to SARS-CoV-2 one year after infection. *Nature* 2021; 595, 426-431 \*co-first author

Bou-Nader C\*, Muecksch F\*, Brown J, Gordon JM, York A, Peng C, Ghirlando R, Summers MF, Bieniasz PD, Zhang J: Structural basis for host tRNA control of HIV-1 Gag localization. *Cell Host Microbe* 2021; 29(9):1421-1436 \*co-first author

Wang Z\*, Schmidt F\*, Weisblum Y\*, Muecksch F\*, Barnes CO\*, Finkin S\*, Schaefer-Babajew D\*, Cipolla M\*, Gaebler C\*, Lieberman JA\*, Oliveira TY, Yang Z, Abernathy ME, Huey-Tubman KE, Hurley A, Turroja M, West KA, Gordon K, Millard KG, Ramos V, Da Silva J, Xu J, Colbert RA, Patel R, Dizon J, Unson-O'Brien C, Shimeliovich I, Gazumyan A, Caskey M, Bjorkman PJ, Casellas R, Hatzioannou T, Bieniasz PD, Nussenzweig MC: mRNA vaccine-elicited antibodies to SARS-CoV-2 and circulating variants. *Nature* 2021; 592, 616-622 \*co-first author

Robbiani DF\*, Gaebler C\*, Muecksch F\*, C Lorenzi JC\*, Wang Z\*, Cho A\*, Agudelo M\*, Barnes CO\*, Gazumyan A\*, Finkin S\*, Häggglöf S, Oliveira TY, Viant C, Hurley A, Hoffmann H-H, Millard KG, Kost RG, Cipolla M, Gordon K, Bianchini F, Chen ST, Ramos V, Patel R, Dizon J, Shimeliovich I, Mendoza P, Hartweger H, Nogueira L, Pack M, Horowitz J, Schmidt F, Weisblum Y, Michailidis E, Ashbrook AW, Waltari E, Pak JE, Huey-Tubman KE, Koranda N, Hoffman PR, West Jr AP, Rice CM, Hatzioannou T, Bjorkman PJ, Bieniasz PD, Caskey M, Nussenzweig MC: Convergent antibody responses to SARS-CoV-2 in convalescent individuals. *Nature* 2020; 584, 437-422 \*co-first author

Muecksch F\*, Citir M\*, Lüchtenborg C, Glass B, Traynor-Kaplan A, Schultz C, Brügger B, Kräusslich HG: Quantification of phosphoinositides reveals strong enrichment of PIP<sub>2</sub> in HIV-1 compared to producer cell membranes. *Sci Rep* 2019; 9, 17661

Muecksch F, Laketa V, Müller B, Schultz C, Kräusslich HG: Synchronized HIV assembly by tunable PIP<sub>2</sub> changes reveals PIP<sub>2</sub> requirement for stable Gag anchoring. *eLife* 2017; 6:e2528

# Integrative Virology

## Fields of Interest

Our work aims at dissecting general principles of host cell biology and immunology that are exploited and hijacked by HIV-1 to cause disease. To this end we apply advanced virology, cell biology and molecular biology techniques to cell systems with physiological relevance ranging from individual primary cell types to organoid and organotypic cell cultures to *in vivo* models.

Part Fackler laboratory:

Our research addresses the cell biology, immunology and pathogenesis of HIV 1 infection with an emphasis on CD4+ T lymphocytes. One focus of our studies is on the molecular mechanisms of action by which the HIV 1 pathogenicity factor Nef reprograms host cell vesicular transport, signal transduction and motility to optimize HIV 1 spread in the host and to accelerate disease progression. Another important aspect of our work is on the host innate immune system in HIV infection and on viral evasion mechanisms. This includes dissecting how the intrinsic immunity factor SERINC5 impairs HIV 1 particle infectivity and how this activity is antagonized by the viral protein Nef, but also studies to elucidate which barriers prevent productive HIV 1 infection of resting CD4+ T lymphocytes. These HIV-related studies involve the development of complex 3D culture systems for studying the relationship between host cell motility and HIV 1 spread in tissue. Finally, we are also interested in the cell biology of CD4 T cell activation and differentiation. In this context, we particularly focus on the newly identified role of nuclear actin filament formation for CD4 T cell help.

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.

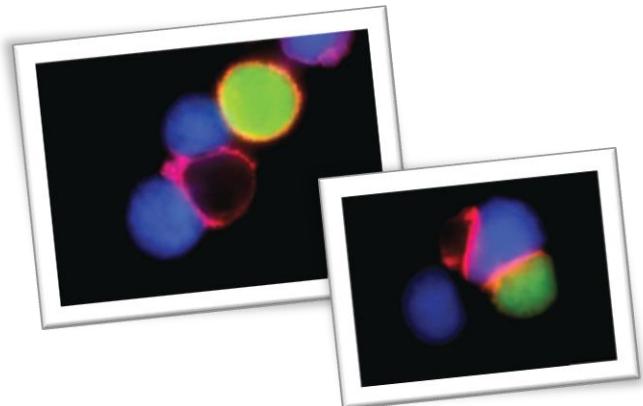
While an overall goal of our laboratory is to explore the specific contributions of nuclear topology and chromatin factors to HIV integration site selection and establishment of latency, we are specifically interested in determining the role of nuclear pore complex proteins in integration site selection. 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
- Adaptive and Innate immunity against HIV-1 and viral evasion thereof
- Synthetic and organotypic 3D models of HIV pathogenesis
- CD4 T cell biology

## Selected Publications

Imle A, Kumberger P, Schnellbächer ND, Fehr J, Carrillo-Bustamante P, Ales J, Schmidt P, Ritter C, Godinez WJ, Müller B, Rohr K, Hamprecht FA, Schwarz US, Graw F, Fackler OT: Experimental and computational analyses reveal that environmental restrictions shape HIV-1 spread in 3D cultures. **Nat Commun.** 2019; 10:2144

Tsopoulidis N, Kaw S, Laketa V, Kutscheidt S, Baarlink C, Stolp B, Grosse R, Fackler OT: T cell receptor-triggered nuclear actin network formation drives CD4+ T cell effector functions. **Sci Immunol** 2019; 4: pii: eaav1987

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Baldauf HM, Stegmann L, Schwarz SM, Ambiel I, Trotard M, Martin M, Burggraf M, Lenzi GM, Lejk H, Pan X, Fregoso Oi, Lim ES, Abraham L, Nguyen L, Rutsch F, König R, Kim B, Emerman M, Fackler OT\* and Keppler OT\*: Vpx overcomes a SAMHD1-independent block to HIV reverse transcription that is specific to resting CD4 T cells. **Proc. Natl. Acad. Sci. USA** 2017; 114: 2729–2734. (\* corresponding authors)

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

Kutscheidt S, Zhu R, Antoku S, Luxton GGW, Stagljar 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, (\* corresponding authors)

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

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

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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-causing parasite *Plasmodium falciparum* proliferates. During this process, *P. falciparum* develops cells that contain multiple nuclei. Typically, when two or more nuclei share the same cytoplasm, they progress synchronously through the cell cycle. However, *P. falciparum* nuclei divide asynchronously despite residing in the same cytoplasm. Using various approaches, including reverse genetics, imaging, and proteomics, the group investigates the molecular mechanisms that drive this non-canonical cell 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 Thomson-Luque lab (MCTU) focuses on the development of novel anti-malaria vaccines and therapies. We are funded by Sumaya-Biotech, and are currently testing a malaria vaccine based on the fIMSP-1 protein which targets both liver and blood stages of the malaria parasite *Plasmodium falciparum*. After a phase Ia carried out in Heidelberg in 2018, we plan to start a phase Ib trial in semi-naïve individuals in Africa together with the SwissTPH and the Ifakara Institute of Health in Tanzania. We are further working on different approaches such as an Adeno6-MSP1 as well as an fIMSP1 mRNA vaccine.

The Ingham lab aims to explore the interaction between parasite development and insecticide resistance in the major malaria vector *Anopheles coluzzii*. The group will specifically concentrate on the impacts of insecticide exposure and the associated changes in oxidative stress levels on the mosquito and how perturbation of this pathway can potentially be exploited for vector control. To achieve these aims, the group will use a variety of techniques including mosquito/parasite phenotyping, RNAseq, RNAi, molecular biology methods and advanced imaging.

The Kilian lab investigates novel secretory organelles generated by malaria parasites to establish host-parasite interaction. The asexual replication of the malaria parasite *Plasmodium falciparum* occurs in the red blood cells of the human host and is responsible for the symptoms and disease severity experienced by patients suffering from malaria tropica. To ensure survival and successful procreation within the organelle-deprived host red blood cells, the parasite reorganizes the cytoplasm of the host cell. This cumulates in the generation of a novel secretory organelle outside the parasite's own cell within the cytoplasm of the host red blood cell. The secretory organelle was named Maurer's clefts in honor of Georg Maurer who thoroughly described the structure in 1902. The Kilian lab aims to decipher this fascinating organelle.

The following teams belong to the Parasitology Unit:

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

-Prof. Dr. Friedrich Frischknecht

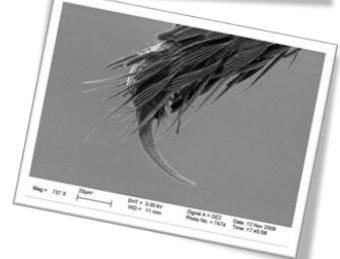
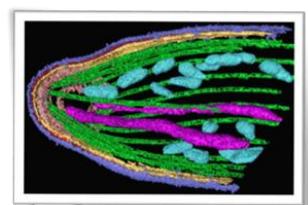
-Dr. Markus Ganter

-Dr. Julien Guizetti

-Dr. Richard Thomson Luque

-Dr. Victoria Ingham

-Dr. Nicole Kilian



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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

Pegoraro S, Duffey M, Otto TD, Wang Y, Rosemann R, Baumgartner R, Fehler SK, Lucantoni L, Avery VM, Moreno-Sabater A, Mazier D, Vial HJ, Strobl S, Sanchez CP, Lanzer M: Erratum: SC83z88 is a clinical development candidate for the treatment of severe malaria. *Nature communications* 2017; 8, 15273

Cyrklaff M, Srismith S, Nyboer B, Burda K, Hoffmann A, Lasitschka F, Adjalley S, Bisseye C, Simpore J, Mueller AK, Sanchez CP, Frischknecht F, Lanzer M: Oxidative insult can induce malaria-protective trait of sickle and fetal erythrocytes. *Nature communications* 2016; 7, 13401

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

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

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

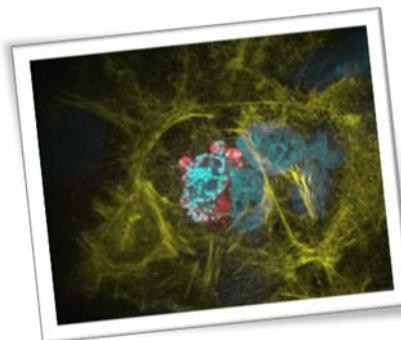
Cyrklaff M, Sanchez CP, Kilian N, Bisseye C, Simpore J, Frischknecht F and Lanzer M: Hemoglobins S and C interfere with actin remodeling in Plasmodium falciparum-infected erythrocytes. *Science* 2011; 334: 1283-1286

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

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

Patra P, Beyer K, Jaiswal A, Battista A, Rohr K, Frischknecht F and Schwarz US: Collective migration reveals mechanical flexibility of malaria parasites. *Nature Physics* 2022; 18, 586-594

Kehrer J, Formaggio P, Muthinja JM, Weber S, Baltissen D, Lance C, Ripp J, Grech J, Meissner M, Funaya C, Amino R and Frischknecht F: Plasmodium sporozoite disintegration during skin passage limits malaria parasite transmission. *EMBO Rep.* 2022; 23(7):e54719

Spreng B, Fleckenstein H, Kübler P, Di Biagio C, Benz M, Patra P, Schwarz US, Cyrklaff M and Frischknecht F: Microtubule number and length determine cellular

shape and function in Plasmodium. *EMBO J.* 2019; 38(15):e100984

Klug D, Frischknecht F: Motility precedes egress of malaria parasites from oocysts. *Elife* 2017; 6, e19157

Cyrklaff M, Frischknecht F, Kudryashev M: Functional insights into pathogen biology from 3D electron microscopy. *FEMS Microbiol Reviews* 2017; 41, 828-853

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 nuclelease-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; 31:357-62

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

Amino R#, Thibierge 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

## Dr. Markus Ganter



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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

Klaus S, Binder P, Kim J, Machado M, Funaya C, Schaaf V, Klaschka D, Kudulyte A, Cyrklaff M, Laketa V, Hoefer T, Guizetti J, Becker N, Frischknecht F, Schwarz US, Ganter M: Asynchronous nuclear cycles in multinucleated Plasmodium falciparum enable rapid proliferation. *Science Advances* 2022; 8(13):eabj5362 PMID:35353560

Schumann R, Bischoff E, Klaus S, Möhring S, Flock J, Keller S, Remans K, Ganter M, Deponte M: Protein abundance and folding rather than the redox state of Kelch13 determine the artemisinin susceptibility of Plasmodium falciparum. *Redox Biology* 2021; 48: 102177 PMID:34773836

Machado M, Steinke S, Ganter M: Plasmodium Reproduction, Cell Size, and Transcription: How to cope with increasing DNA content? *Front Cell Infect Microbiol* 2021; 11, 660679 PMID: 33898332

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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, Duraisingham 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, Duraisingham MT. Parasite calcineurin regulates host cell recognition and attachment by apicomplexans. *Cell Host Microbe* 2015; 18, 49-60

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

## Dr. Julien Guizetti



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## Scientific Vita

2017-present: 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

Klaus S, Binder P, Kim J, Machado M, Funaya C, Schaaf V, Klaschka D, Kudulyte A, Cyrlkaff M, Laketa V, Höfer T, Guizetti J, Becker NB, Frischknecht F, Schwarz US and Ganter M: Asynchronous nuclear cycles in multinucleated Plasmodium falciparum facilitate rapid proliferation. *Sci Adv* 2022; 13:eabj5362

Simon CS, Funaya C, Bauer J, Voß Y, Machado M, Penning A, Klaschka D, Cyrlkaff M, Kim J, Ganter M and Guizetti J: An extended DNA-free intranuclear compartment organizes centrosome microtubules in malaria parasites. *Life Sci Alliance* 2021; 4(11):e202101199

Simon CS, Stürmer VS & Guizetti J: How Many Is Enough? - Challenges of Multinucleated Cell Division in Malaria Parasites. *Front Cell Infect Microbiol* 2021; 11, 658616

Mehnert AK, Simon CS and Guizetti J: Immunofluorescence staining protocol for STED nanoscopy of Plasmodium-infected red blood cells. *Mol Biochem Parasitol.* 2019; 229, 47-52

Bryant JM, Regnault C, Scheidig-Benatar C, Baumgarten S, Guizetti J\* and 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 and Scherf A: Trans-acting GC-rich non-coding RNA at var expression site modulates gene counting in malaria parasite. *Nucleic Acids Res* 2016; 44, 9710-9718

Guizetti J, Martins RM, 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, Müller-Reichert T and Gerlich DW: Cortical constriction during abscission involves helices of ESCRT-III-dependent filaments. *Science* 2011; 331, 1616-1620

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

## Dr. Victoria Ingham



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## Scientific Vita

2020-present: DZIF Group Leader, Parasitology Unit, Heidelberg University Hospital

2017-2020: MRC Skills Development Fellow, Vector Biology, Liverpool School of Tropical Medicine, UK

2018: Visiting Scientist, The Broad Institute, Boston, USA

2017: Visiting Scientist, Harvard TH Chan School of Public Health, Boston, USA

2016-2017: Post-Doctoral Research Associate, Vector Biology, Liverpool School of Tropical Medicine, UK

2012-2016: PhD, University of Warwick, UK

2011-2012: MSc Systems Biology, University of Warwick, UK

2008-2011: MA Biological Sciences, University of Oxford, UK

## Specific Research Interests

- Molecular mechanisms of insecticide resistance
- Vector – parasite interactions
- Transcription factor control
- Transcriptomics and Genomics
- Integration of informatics with molecular biology

## Selected Publications

Ingham VA, Elg S, Nagi SC, Dondelinger F: Capturing the transcription factor interactome in response to sub-lethal insecticide exposure. *bioRxiv* 2020; 39969

Ingham VA, Brown F, Ranson H: Sub-lethal pyrethroid exposure and ageing lead to pronounced changes in gene expression in insecticide resistance *Anopheles coluzzii*. *bioRxiv* 2020; 250852

Brown F, Paton DG, Catteruccia F, Ranson H and Ingham VA: Steroid hormone agonists reduce female fitness in insecticide-resistant *Anopheles* populations. *Insect Biochem Mol Biol* 2020; 121:103372

Ingham VA, Bennett A, Peng D, Wagstaff SC, Ranson H: IR-TEX: An open source data integration tool for big data transcriptomics designed for the major malaria vector *Anopheles gambiae*. *J Vis Exp* 2020; 155

Minetti C, Ingham VA, Ranson H: Effects of insecticide resistance and exposure on *Plasmodium* development in *Anopheles* mosquitoes. *Curr Opin Insect Sci* 2020; 39:42-49

Ingham VA, Anthousi A, Douris V, Harding NJ, Lycett G, Morris M, Vontas J, Ranson H: A sensory appendage protein protects malaria vectors from pyrethroids. *Nature* 2020; 577(7790):376-380

Ingham VA, Wagstaff S and Ranson H: Transcriptomic meta-signatures identified in *Anopheles gambiae* populations reveal previously undetected insecticide resistance mechanisms. *Nat Commun* 2018; 9:5282

Ingham VA, Pignatelli P, Moore JD, Wagstaff S, Ranson H: The transcription factor *Maf-S* regulates metabolic resistance to insecticides in the malaria vector *Anopheles gambiae*. *BMC Genomics* 2017; 30;18(1):669

Pignatelli P, Ingham VA, Balabanidou V, Vontas J, Lycett G, Ranson H: The *Anopheles gambiae* ATP-binding cassette transporter family: phylogenetic analysis and tissue localization provide clues on function and role in insecticide resistance. *Insect Mol Biol* 2018; 27(1):110-122

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## Dr. Richard Thomson Luque



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 Web: <https://www.klinikum.uni-heidelberg.de/zentrum-fuer-infektiologie/parasitology-unit/research/sumaya-lab>

## Scientific Vita

2021-present: Junior Group Leader at MCTU, Center for Infectious Diseases-Parasitology Heidelberg University Hospital, Heidelberg / Chief Scientific Officer / Sumaya-Biotech

2018-2022: PhD, Biochemistry, Molecular Biology and Biomedicine, Universidad Complutense de Madrid, Spain, Madrid

2017-2021: Marie Skłodowska Curie- Postdoctoral Fellow, Center for Infectious Diseases-Parasitology Heidelberg University Hospital, Heidelberg

2014-2017: Research Associate, University of South Florida College of Public HealthTampa, Florida, USA

2013-2014: GSK OpenLab Fellowship. Fundação de Medicina Tropical Heitor Vieira Dourado (FMT-HVD) Manaus, Amazonas, Brasil

2012-2013: Medical Research Fellow at Institut de Salut Global de Barcelona ISGLOBAL (CRESIB), Spain Barcelona

2007-2010: Master of Science (MSc), Structure and function of proteins, Biochemistry and Molecular Biology, Universitat Autònoma of Barcelona, Spain

2007-2010 Emergency Lab Staff Hospital Universitari Germans Trías i Pujol, Barcelona, Spain

2003-2007: MD Residency Clinical Biochemistry HUGTiP, Barcelona, Spain

2001-2002: Master of Science (MSc), Tropical Medicine and International Health, Universitat Autònoma of Barcelona, Spain

1995-2001: Studies in Medicine and Surgery, University of Málaga, Spain

## Specific Research Interests

- Malaria cell biology and physiopathology
- Immunology and vaccine development
- Plasmodium vivax malaria
- Reticulocytes and erythropoiesis

## Selected Publications

Thomson-Luque R, Votborg-Novél L, Ndovie W, Andrade CM, Niangaly M, Attipa C, Lima NF, Coulibaly D, Doumtabe D, Guindo B, Tangara B, Maiga F, Kone AK, Traore K, Kayentao K, Ongoiba A, Doumbo S, Thera MA, Traoré B, Seydel K, Osório NS and Portugal S: Plasmodium falciparum transcription in different clinical presentations of

malaria associates with circulation time of infected erythrocytes. *Nat Commun.* 2021; 12(1):4711

Thomson-Luque R and Bautista JM: Home Sweet Home: Plasmodium vivax-Infected Reticulocytes-The Younger the Better? *Front Cell Infect Microbiol* 2021; 11:675156

Andrade CM, Fleckenstein H, Thomson-Luque R, Doumbo S, Lima NF, Anderson C, Hibbert J, Hopp CS, Tran TM, Li S, Niangaly M, Cisse H, Doumtabe D, Skinner J, Sturdevant D, Ricklefs S, Virtaneva K, Asghar M, Homann MV, Turner L, Martins J, Allman EL, N'Dri ME, Winkler V, Llinás M, Lavazec C, Martens C, Färnert A, Kayentao K, Ongoiba A, Lavstsen T, Osório NS, Otto TD, Recker M, Traore B, Crompton PD and Portugal S: Increased circulation time of Plasmodium falciparum underlies persistent asymptomatic infection in the dry season. *Nat Med.* 2020; (12):1929-1940

Thomson-Luque R, Wang C, Ntumngia CB, X S, Szekeres K, Conway A, Adapa SR, Barnes SJ, Adams JH and Jiang RHY: In depth phenotypic characterization of reticulocyte maturation using mass cytometry. *Blood Cells Mol Dis* 2018; 72:22-33

Roth A, Maher SP, Conway AJ, Ubalee R, Chaumeau V, Andolina C, Kaba SA, Vantaux A, Bakowski MA, Thomson-Luque R, Adapa SR, Singh N, Barnes SJ, Cooper CA, Rouillier M, McNamara CW, Mikolajczak SA, Sather N, Witkowski B, Campo B, Kappe SHI, Lanar DE, Nosten F, Davidson S, Jiang RHY, Kyle DE and Adams JH: A comprehensive model for assessment of liver stage therapies targeting Plasmodium vivax and Plasmodium falciparum. *Nat Commun.* 2018; 9:1837

Ntumngia FB, Thomson-Luque R, Galusic S, Frato G, Frischmann S, Peabody DS, Chackerian B, Ferreira MU, King CL and Adams JH: Identification and immunological characterization of the ligand domain of Plasmodium vivax reticulocyte binding protein 1a. *J Infect Dis* 2018; 218(7):1110-1118

Ntumngia FB, Pires CV, Barnes SJ, George MT, Thomson-Luque R, Kano FS, Alves JRS, Ursuova D, Pereira DB, Tolia NH, King CL, Carvalho LH and Adams JH: An engineered vaccine of the Plasmodium vivax Duffy binding protein enhances induction of broadly neutralizing antibodies. *Sci Rep* 2017; 7(1):13779

Thomson-Luque R, Saliba KS, Kocken CH and Pasini EM: A Continuous, Long-Term Plasmodium Vivax In Vitro Blood-Stage Culture: What Are We Missing? *Trends Parasitol* 2017; 33(12):921-924

Ntumngia FB, Thomson-Luque R, Torres L de M, Gunalan K, Carvalho LH and Adams JH: A Novel Erythrocyte Binding Protein of Plasmodium vivax Suggests an Alternate Invasion Pathway into Duffy-Positive Reticulocytes. *mBio.* 2016; 7(4):e01261-16

Shaw-Saliba K\*, Thomson-Luque R\*, Obaldía N, Nuñez M, Dutary S, Lim C, Barnes S, Kocken CHM, Duraisingham MT, Adams JH and Pasini EM: Insights into an Optimization of Plasmodium vivax Sal-1 In

Vitro Culture: The Aotus Primate Model. *PLoS Negl Trop Dis.* 2016; 10(7):e0004870

## Dr. Nicole Kilian



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## Scientific Vita

2022-present: Research Group Leader, Centre for Infectious Diseases, Parasitology, Heidelberg University Hospital

2019-present: Habilitation Candidate, Centre for Infectious Diseases, Parasitology, Heidelberg University Hospital

2018-2019: Postdoctoral Associate, Department of Infectious Diseases, Yale School of Medicine, Yale University

2013-2018: Postdoctoral Associate, Department of Cell Biology, Yale School of Medicine, Yale University

2008-2013: PhD Thesis, Centre for Infectious Diseases, Parasitology, Heidelberg University Hospital

2007-2008: Diploma Thesis, Centre for Infectious Diseases, Parasitology, Heidelberg University Hospital

2003-2008: Studies of Biology, Heidelberg University

## Specific Research Interests

- Novel secretory organelles of parasite origin
- Host – parasite interaction
- Malaria diagnosis

## Selected Publications

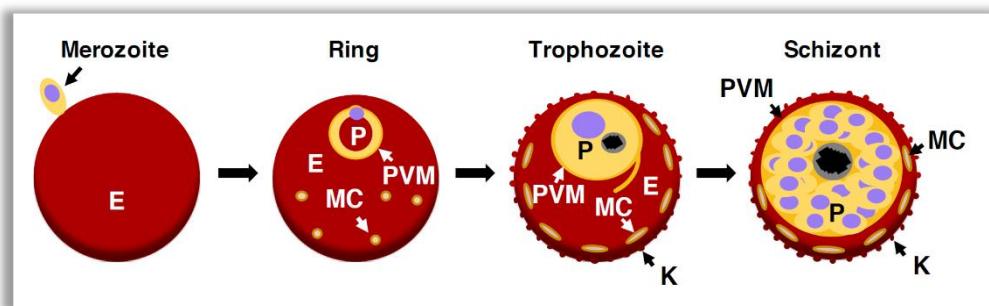
Broichhagen JT and Kilian N<sup>†</sup>: Chemical Biology Tools to Investigate Malaria Parasites. *ChemBioChem* 2021; 22(13):2219-2236. Review article.

Kilian N<sup>†</sup>, Zhang Y, LaMonica L, Hooker G, Toomre D, Ben Mamoun C<sup>†</sup> and Ernst AM<sup>†</sup>: Palmitoylated Proteins in Plasmodium falciparum-Infected Erythrocytes: Investigation with Click Chemistry and Metabolic Labeling. *Bioessays* 2020; 42(6)

Gitta B<sup>†</sup> and Kilian N<sup>†</sup>: Diagnosis of Malaria Parasites Plasmodium spp. in Endemic Areas: Current Strategies for an Ancient Disease. *Bioessays* 2020; 42(1). Review article

Abraham A, Brasov I, Thekkiniath J, Kilian N, Lawres L, Gao R, DeBus K, He L, Yu X, Zhu G, Graham M, Liu X, Molestina R and Ben Mamoun C: Establishment of a Continuous in vitro Culture of Babesia duncani in Human Erythrocytes Reveals Unusually High Tolerance to Recommended Therapies. *J Biol Chem* 2018; 293(52):19974-19981

Kilian N, Choi JY, Voelker DR and Ben Mamoun C: Role of Phospholipid Synthesis in the Development and Differentiation of Malaria Parasites in the Blood". *J Biol Chem* 2018; 293(45):17308-17316. Review article



Kilian N\*, Goryaynov A\*, Lessard MD, Hooker G, Toomre D, Rothman JE and Bewersdorf J: Assessing Photodamage in Live-Cell STED Microscopy. *Nat Methods* 2018; (10):755-756

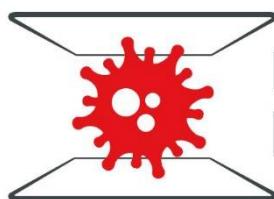
Thekkiniath J, Kilian N, Lawres L, Gewirtz MA, Graham MM, Liu X, Ledizet M and Ben Mamoun C: Evidence for Vesicle-Mediated Antigen Export by the Human Pathogen Babesia microti. *Life Sci Alliance* 2019; 2(3):e201900382

Kilian N\*, Sirismith S\*, Dittmer M, Ouermi D, Bisseye C, Simpore J, Cyrklaff M, Sanchez CP and Lanzer M: Hemoglobins S and C Affect Protein Export in

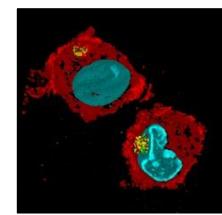
Plasmodium falciparum-Infected Erythrocytes. *Biology Open* 2015; 4(3):400-10

Kilian N\*, Dittmer M\*, Cyrklaff M, Ouermi D, Bisseye C, Simpore J, Frischknecht F, Sanchez CP and Lanzer M: Hemoglobin S and C Affect the Motion of Maurer's Clefts in Plasmodium falciparum-Infected Erythrocytes. *Cell Microbiol* 2013; (7):1111-26

Cyrklaff M, Sanchez CP, Kilian N, Bisseye C, Simpore J, Frischknecht F and Lanzer M: Hemoglobins S and C Interfere with Actin Remodeling in Plasmodium falciparum-Infected Erythrocytes. *Science* 2011; 334(6060):1283-6



# Infectious Diseases IMAGING PLATFORM



## Fields of Interest

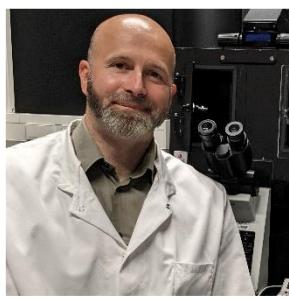
The physiology of host-pathogen interactions is governed by individual, stochastic and often rare molecular events. For example, latent HIV infections occur only in one in a million CD4+ T cells in vivo, HCV will only replicate in one out of hundred thousand hepatocyte-derived cells etc. Although, classical biochemical, genetic and genomic approaches have been employed over the years to yield important insights in host-pathogen interactions, most of these experimental approaches are population-based ("bulk"), end-point analyses where obtained information represents an average across the population and where important parameters can be missed as they become "averaged out" in the bulk measurement. To truly understand the differences between the health and the disease state, we need to employ an experimental approach that is able to identify and quantitatively examine these individual molecular events. With the recent technological innovations, microscopy has emerged as an ideal approach to accomplish this task.

Besides providing the required spatial resolution, modern microscopy is able to quantitatively assess complex dynamics of a biological system and provide the most realistic representation of a living system. For this reason, we established Infectious Disease Imaging Platform (IDIP) – an advanced light microscopy infrastructure placed under enhanced biosafety containment (BSL2 and BSL3). The infrastructure consists of 15+ microscopy systems, 5 instruments for electron microscopy sample preparation, FACS, tailored IT infrastructure as well as sample preparation area, image analysis infrastructure and dedicated expert personnel. This comprehensive microscopy infrastructure enables imaging of pathogens across a wide range of spatiotemporal scales and organizational levels of complexity under close-to-physiological setting.

The Infectious Diseases Imaging Platform is run by:

-Dr. Vibor Laketa

## Dr. Vibor Laketa



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Web: <https://www.idip-heidelberg.org/>

## Scientific Vita

2018-present Head of Infectious Disease Imaging Platform (IDIP), Center for Integrative Infectious Diseases Research (CIID), University Hospital Heidelberg

2013-present Imaging platform coordinator in German Center for Infection Research (DZIF), Heidelberg, Germany

2008-2013 Staff Scientist, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany

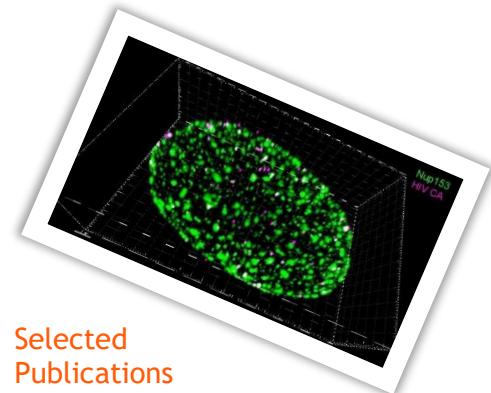
2006-2008 PostDoc, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany

2002-2006 Dr. rer. nat. (summa cum laude), European Molecular Biology Laboratory (EMBL) and Heidelberg University, Germany

1997-2002 MSc. Molecular Biology, University of Zagreb, Croatia and Ludwig Institute for Cancer Research, Uppsala, Sweden

## Specific Research Interests

- Advanced light and electron microscopy infrastructure to examine pathophysiological processes in infectious diseases at different spatiotemporal scales and organizational complexities
- Development of automated microscopy workflows for data acquisition, processing and analysis
- Development of microscopy-based assays and procedures used in infectious disease research, drug screening and diagnostics



## Selected Publications

Heuss C, Rothhaar P, Burm R, Lee JY, Ralfs P, Haselmann U, Ströh LJ, Colasanti O, Tran CS, Schäfer N, Schnitzler P, Merle U, Bartenschlager R, Patel AH, Graw F, Krey T, Laketa V, Meuleman P, Lohmann V: A Hepatitis C virus genotype 1b post-transplant isolate with high replication efficiency in cell culture and its adaptation to infectious virus production in vitro and in vivo. *PLoS Pathog.* 2022; 18(6):e1010472

Cortese M, Laketa V: Advanced microscopy technologies enable rapid response to SARS-CoV-2 pandemic. *Cell Microbiol.* 2021; 23(7):e13319

Klein S, Wimmer WH, Winter SL, Kolovou A, Laketa V, Chlanda P: Post-correlation on-lamella cryo-CLEM reveals the membrane architecture of lamellar bodies. *Communications Biology* 2021; 29(41):137

Müller TG, Zila V, Peters K, Schifferdecker S, Stanic M, Lucic B, Laketa V, Lusic M, Müller B, Kräusslich HG: HIV-1 uncoating by release of viral cDNA from capsid-like structures in the nucleus of infected cells. *Elife* 2021; 27:10:e64776

Pape C, Remme R, Wolny A, Olberg S, Wolf S, Cerrone L, Cortese M, Klaus S, Lucic B, Ullrich S, Anders-Össwein M, Wolf S, Cerikan B, Neufeldt CJ, Ganter M, Schnitzler P, Merle U, Lusic M, Boulant S, Stanifer M, Bartenschlager R, Hamprecht FA, Kreshuk A, Tischer C, Kräusslich HG, Müller B, Laketa V: Microscopy-based assay for semi-quantitative detection of SARS-CoV-2 specific antibodies in human sera. *Bioessays* 2021; 43(3):e2000257

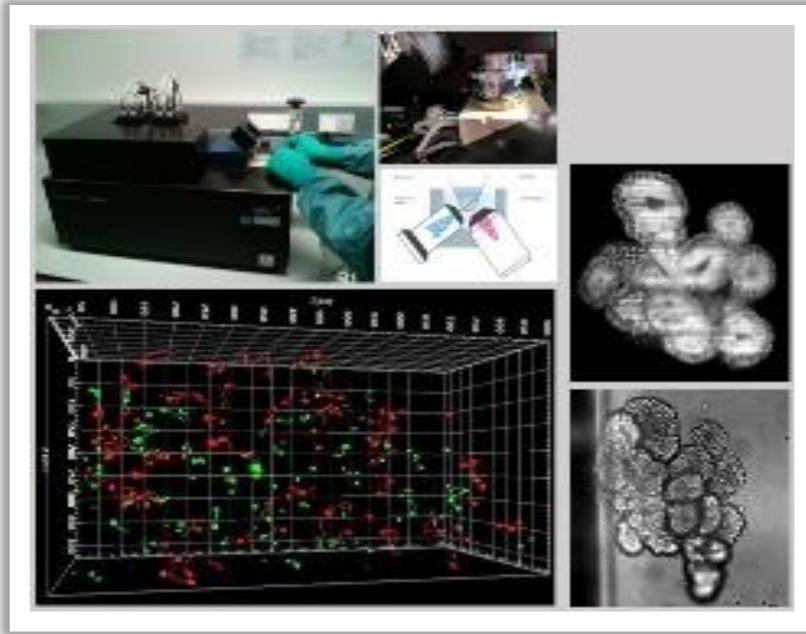
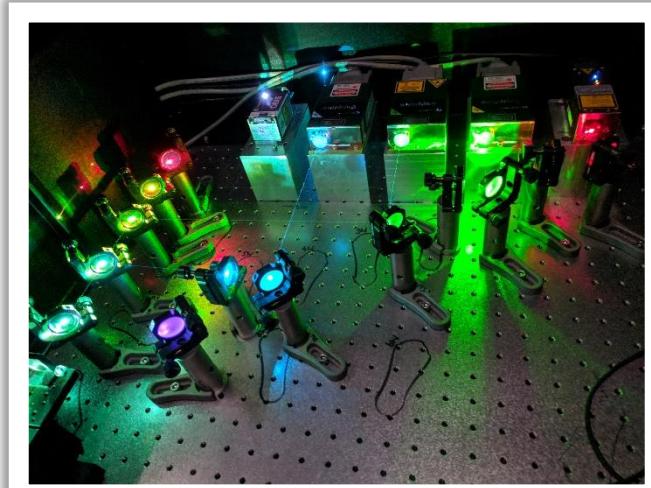
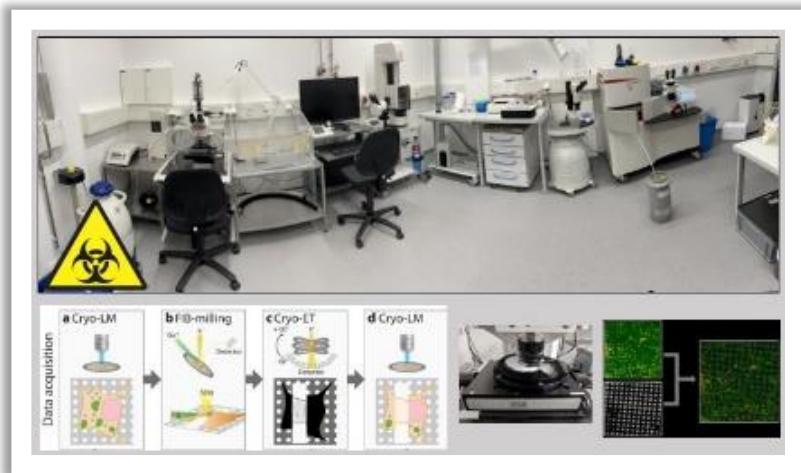
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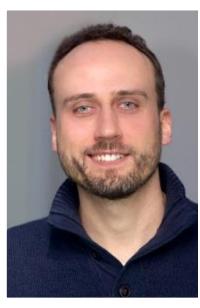
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# List of the Associated Research Groups Major Infectious Diseases



**Dr. Marco Binder**

Research Group "Dynamics of early viral infection and the innate antiviral response"  
F170, INF 242, 69120 Heidelberg  
Phone: +49 6221 424974  
Email: m.binder@dkfz.de  
Web: <http://www.dkfz.de/en/virus-assoziierte-karzinogenese/groups/AGBinder>

## 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. Prof. Dr. Martin Müller**

Research Group "Tumorvirus-specific vaccination strategies"  
Fo35, INF 280, 69120 Heidelberg  
Phone: +49 6221 424628  
Email: martin.mueller@dkfz.de  
Web: <http://www.dkfz.de/en/fo35/>

## 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



### PD Dr. Ellen Krautkrämer

Research Group "Hantavirus pathogenesis"  
Nephrology, INF 162, 69120 Heidelberg, University of Heidelberg  
Phone: +49 6221 9112 0  
Email: ellen.krautkraemer@med.uni-heidelberg.de  
Web: <http://nierenzentrum-heidelberg.com>

#### 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

Research Group "Immunotherapy and Immunoprevention"  
F130, INF 242; 69120 Heidelberg  
Phone: +49 6221 423820  
Email: a.riemer@dkfz.de  
Web: <http://www.dkfz.de/en/immuntherapie-immunpraevention/index.php>

#### 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



### apl. Prof. Dr. Martin Löchelt

Research Group "Molecular Biology and Application of Recombinant Foamy Viruses"  
Fo20, INF 280, 69120 Heidelberg  
Phone: +49 6221 424933  
Email: m.loechelt@dkfz.de  
Web: <http://www.dkfz.de/en/fo20/groups/loechelt/index.html>

### 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. Felix Hoppe-Seyler

Research Group "Molecular Therapy of Virus-Associated Cancers"  
Fo65, INF 242, 69120 Heidelberg  
Phone: +49 6221 424872  
Email: hoppe-seyler@dkfz.de  
Web: <https://www.dkfz.de/en/fo65/>

### Specific Research Interests

- Human papillomavirus (HPV)-linked cancers: Transformation mechanisms and novel therapeutic strategies
- Crosstalk between HPVs and the host cell metabolism (hypoxia, iron and glucose metabolism)
- Cell biology of HPV-positive cancer cells: Regulation of senescence and apoptosis
- Signal transduction



### Prof. Dr. Hedda Wardemann

Research Group "B Cell Immunology / B-Zell-Immunologie" (D130)  
INF 280, 6. Stock, 69120 Heidelberg  
Phone: +49 6221 42 1270  
Email: h.wardemann@dkfz-heidelberg.de  
Web: <https://www.dkfz.de/en/b-zell-immunologie/index.php>

#### 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

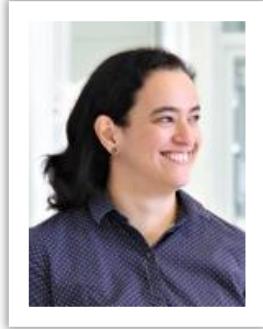


### Dr. Erec Stebbins

Research Group "Structural Biology of Infection and Immunity" (D160)  
INF 280, H2.07.069, 69120 Heidelberg  
Phone: +49 6221 421380  
Email: e.stebbins@dkfz-heidelberg.de  
Web: <https://www.dkfz.de/en/strukturbio-infektion-immunitaet/index.php>

#### 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

Research Group "Immune Diversity" (D150)  
INF 280, H2.07.072  
69120 Heidelberg  
Phone: +49 6221 421390  
Email: n.papavasiliou@dkfz-heidelberg.de  
Web: <https://www.dkfz.de/en/immundiversitaet/index.php>

#### 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



### Prof. Dr. Yvonne Samstag

*Section Molecular Immunology*  
Immunologie, INF 305, 69120 Heidelberg  
Phone: +49 6221 56 4039  
Email: [yvonne.samstag@urz.uni-heidelberg.de](mailto:yvonne.samstag@urz.uni-heidelberg.de)  
Web: <http://www.klinikum.uni-heidelberg.de/Sektion-Molekulare-Immunologie.2831.o.html>

#### Specific Research Interests

- Regulation of immune responses by the micromilieu (human and mouse models)
- Co-stimulatory signaling in T lymphocytes, cytoskeletal remodeling and redox regulation
- Regulation and function of granulocytes
- Allergy and chronic inflammatory diseases (SFB TRR 156)
- Tumor immunology and immune therapy (CAR T-cells, Checkpoint inhibitors)
- Tumor migration and metastasis
- Immunomodulation by plant-derived substances ([www.azkim.de](http://www.azkim.de), [www.cimresearch.org](http://www.cimresearch.org))
- High resolution imaging, InFlow microscopy



### Dr. Frederik Graw

Research Group "Modelling Infection & Immunity"  
BioQuant-Center for Quantitative Biology  
INF 267, 69120 Heidelberg  
Phone: +49 6221 54 51309  
Email: [frederik.graw@bioquant.uni-heidelberg.de](mailto:frederik.graw@bioquant.uni-heidelberg.de)  
Web: <http://www.bioquant.uni-heidelberg.de/research/groups/modelling-infection-immunity.html>

#### Specific Research Interests

- Mathematical modeling of host-pathogen interactions
- Spatio-temporal dynamics of infection and immune processes
- Viral spread within tissues
- Immune cell differentiation and vaccine design



### Prof. Dr. Frank Rösl

Division of Viral Transformation Mechanisms  
DKFZ, INF 280, 69120 Heidelberg  
Phone: +49 6221 424901  
Email: [f.roesl@dkfz.de](mailto:f.roesl@dkfz.de)  
Web: <https://www.dkfz.de/en/fo30/index.php>

#### Specific Research Interests

- Interference of papillomaviruses in signal transduction pathways
- relationship between "white" skin cancer and the infection with so-called cutaneous papilloma viruses



### Prof. Dr. Dr. Christine E. Engeland

Research Group "Mechanisms of Oncolytic Immunotherapy"

Clinical Cooperation Unit Virotherapy

F230, Im Neuenheimer Feld 242, 69120 Heidelberg

Phone: +49 6221 42 4931

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Web: <https://www.dkfz.de/en/virotherapie/index.php>

or

Faculty of Health, Witten/Herdecke University, Stockumer Str. 10, 58453 Witten

Phone: +49 2302 – 926290

Email: [Christine\\_Engeland@uni-wh.de](mailto:Christine_Engeland@uni-wh.de)

Web: <https://www.uni-wh.de/gesundheit/department-fuer-humanmedizin/lehrstuehle-institute-und-zentren/lehrstuhl-fuer-virologie-und-mikrobiologie/professur-fuer-experimentelle-virologie>

### Specific Research Interests

- viral vectors for cancer immunotherapy and vaccination
- measles virus (vaccines) and paramyxoviruses
- virus-host interactions



### Prof. Dr. Adelheid Cerwenka

Angeborene Immunität

Centrum für Biomedizin und Medizintechnik Mannheim, Ludolf Krehl-Straße 13-17

68167 Mannheim

Phone: +49 621 383 71504

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Web: <https://www.umm.uni-heidelberg.de/forschung/forschungsschwerpunkte/onkologie/mitglieder/prof-dr-adelheid-cerwenka/>

### Specific Research Interests

- Molecular mechanism of NK/ILC activation
- Functional Diversification of NK cells
- Interaction of NK/ILCs with other Immune Cells, Endothelial Cells and virus-infected Liver Cells
- novel NK Cell-based Immunotherapies and Combination Therapies in preclinical Mouse Models

# Former group leaders of the Major Infectious Diseases

!Practicals/master theses that are completed in these working groups are considered external and must be applied for separately!



## Dr. Silvia Portugal

Max-Planck-Institut für Infektionsbiologie  
Charitéplatz 1; Campus Charité Mitte  
10117 Berlin, Germany  
Web: <https://www.mpiib-berlin.mpg.de/2019364/malaria-parasite-biology>

### Specific Research Interests

- *Plasmodium* seasonal transmission
- Survival mechanisms of *P. falciparum* when no vectors are available
- Immune response to asymptomatic *P. falciparum* infections
- *Plasmodium* virulence and variant surface antigens
- *Plasmodium* gametocytogenesis dynamics throughout the dry season
- Transmission capacity of *P. falciparum* kept asymptotically during the dry season



## Dr. Ross G. Douglas

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Web: <https://www.uni-giessen.de/fbz/fbog/institute/ernaehrungswissenschaft/prof/becker/forschung>

### Specific Research Interests

- *Plasmodium* cytoskeleton dynamics



## Dr. Pierre-Yves Lozach

INRAE-University Lyon 1  
50 Avenue Tony Garnier  
69007 Lyon, France  
Email: [pierre-yves.lozach@univ-lyon1.fr](mailto:pierre-yves.lozach@univ-lyon1.fr)  
Web: [www.lozachlab.com](http://www.lozachlab.com)

### Specific Research Interests

- amyloid fibril proteins
- arbovirus
- cell biology of virus entry
- early virus–host cell interactions
- emerging zoonotic viruses
- molecular factors responsible for viral virulence
- viral fusion
- virus–receptor interactions

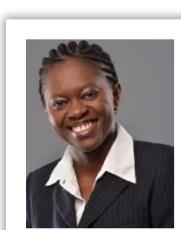


## Prof. Dr. Jude Przyborski

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Web: <https://www.uni-giessen.de/fbz/fbog/institute/ernaehrungswissenschaft/prof/becker>

### Specific Research Interests

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



## Prof. Dr. Faith Osier

IAVI Human Immunology Laboratory  
Chelsea & Westminster NHS Foundation Trust  
369 Fulham Road, London SW10 9NH, UK  
Phone: +44 (0) 7434 764077  
Email: [FOsier@iavi.org](mailto:FOsier@iavi.org)  
Web: <https://www.imperial.ac.uk/infectious-disease/research/immunology-infection/human-immunology/>

### Specific Research Interests

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

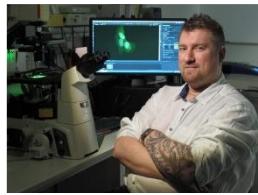


## Dr. Megan Stanifer

University of Florida Medical School  
Department of Molecular Genetics and Microbiology  
Gainesville, Florida, USA  
Email: [m.stanifer@ufl.edu](mailto:m.stanifer@ufl.edu)  
Web: <http://mgm.ufl.edu/profile/stanifer-megan/>

### Specific Research Interests

- Response of epithelial cells (lung and gut) to virus infections
- Role of type I and III interferons in controlling virus infection at mucosal surfaces
- Evaluating single cell immune responses to virus infection
- Establishing microfluidics to better mimic the host cell environment

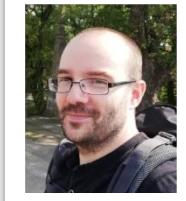


### Dr. Steeve Boulant

Department of Molecular Genetics & Microbiology  
 University of Florida College of Medicine  
 P.O. Box 100266  
 Gainesville, FL 32610-0266  
 Phone: 352-273-6380  
 Email: s.boulant@ufl.edu  
 Web: <https://www.boulantlab.com/>  
<http://mgm.ufl.edu/faculty/>

#### Specific Research Interests

- Enteric viruses (*Astrovirus, Rotavirus, Norovirus*)
- Human Intestinal organoids
- Response of human intestinal epithelial cell to enteric viruses
- Mechanisms of enteric virus pathogenesis
- Single cell sequencing characterization of host/pathogen interaction
- Importance of low oxygen conditions (hypoxia) in regulating gut homeostasis
- System virology



### Dr. Sébastien Boutin

Klinik für Infektiologie und Mikrobiologie  
 Universität zu Lübeck  
 Phone: +4945131019030  
 Email: sebastien.boutin@uni-luebeck.de  
 Web: tba

#### Specific Research Interests

- Human microbiome
- Airways infection
- Host-microbes interactions
- Microbial ecology and evolution
- Next-generation sequencing



### Prof. Dr. med. Dennis Nurjadi

Klinik für Infektiologie und Mikrobiologie  
 Universität zu Lübeck  
 Phone: +4945131019011  
 Email: dennis.nurjadi@uni-luebeck.de  
 Web: tba

#### Specific Research Interests

- Immune mechanisms and pathogen-host interaction of *Staphylococcus aureus* colonization and infection
- Molecular mechanisms and epidemiology of antimicrobial resistance in clinically relevant pathogens
- NGS-based strain typing and (bacterial) outbreak diagnostics
- Clinical studies in infectious diseases

## Students of the Major ‘Infectious Diseases’ WS 2016-2017



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.

## Students of the Major ‘Infectious Diseases’ WS 2017-2018



From left to right, in the back: Martin Kampmann, Patrick Küber, Annika Binder, Ann-Kathrin Mehnert, Nora Heber, Philipp Ehmann, Simay Ayhan. In the front: Camila Metz, Katharina Morath, Michelle Yee, Hannah van Dijk

## Students of the Major ‘Infectious Diseases’ WS 2018-2019



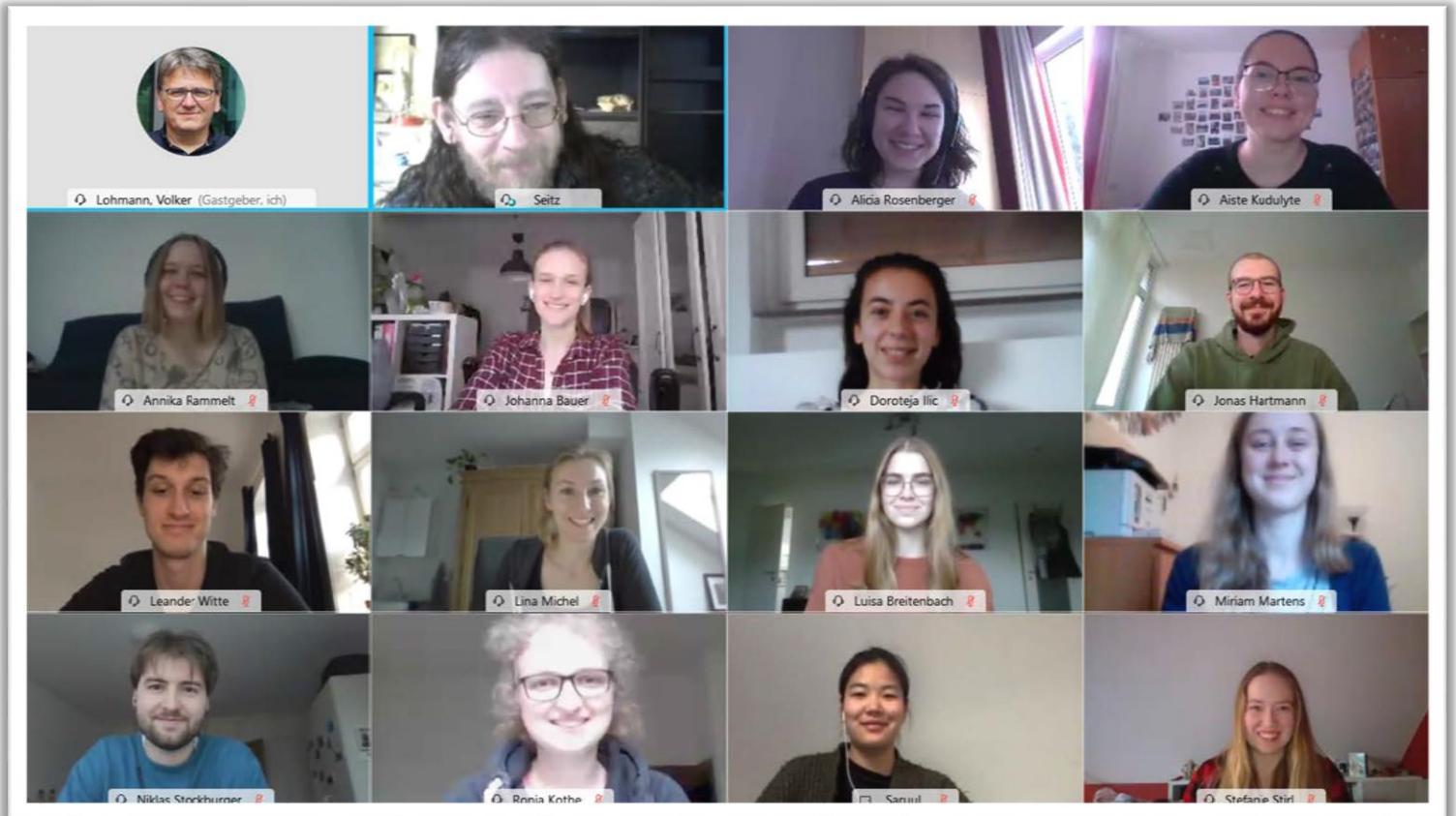
From left to right, in the back: Stefan Diehl, Nikolay Sergeev, Valerii Martynov, Noah Ruf, Jose Luis Guzman Martin, Felix Pahmeier. In the front: Chia Ching Wu, Hao-En Huang, Dorothee Reuß, Laura Emig, Lisa Augstein, Carmen Lahr, Marta Freixas Teres

## Students of the Major ‘Infectious Diseases’ WS 2019-2020



From left to right, in the back: Carl-Niklas Schneider, Romy Brecht, Nathan Ribot, Christoph Wenz, Vidmante Visockaite. In the front: Mariana Ríos Vázquez, Antonia Louisa Boehmert, Koleta Michalek, Sara Kraker, Paulina Schad, Sarah Peterl, Charlotte Kamm.

## Students of the Major 'Infectious Diseases' WS 2020-2021



From left to right and from top to bottom: Alicia Rosenberger, Aiste Kudulyte, Annika Rammelt, Johanna Bauer, Doroteja Ilic, Jonas Hartmann, Leander Witte, Lina Michel, Luisa Breitenbach, Miriam Martens, Niklas Stockburger, Ronja Kothe, Saruul Jargalsaikhan, Stefanie Stirl.

## Students of the Major ‘Infectious Diseases’ WS 2021-2022



From left to right, in the back: En-Jui Cho, Maren Gehringer, Vera Lechner, Claudia Bastl, Pia Hüber. In the front: Argyris Satikidis, Simon Kneilmann, Sophie Stopper, Lea Juliane Woltereck, Katharina Röver.