



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 (www.trr179.de),

TRR319 (<https://rmap.uni-mainz.de/>),

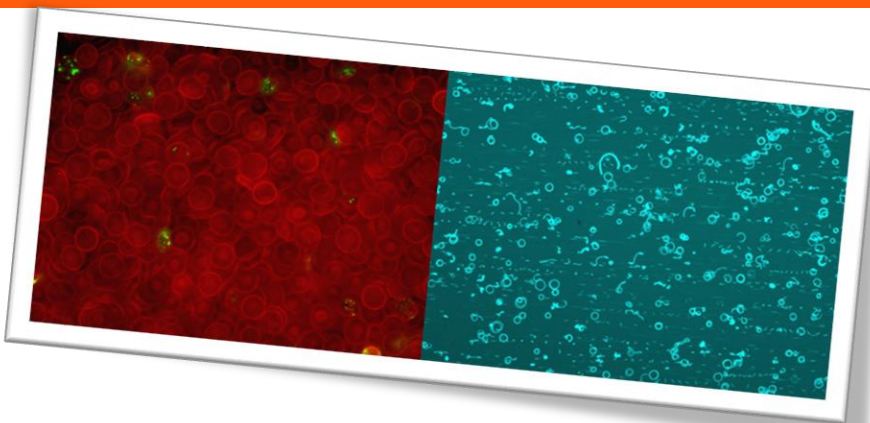
TRR186 (<https://trr186.uni-heidelberg.de/>).

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".



Heidelberg Bachelor courses "Biology" and "Molecular and Cellular Biology" who are interested in this Major are advised to attend the lectures and courses on microbiology, infectious disease immunology, parasitology and virology in Semesters 4 and 5.

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.

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

Acquired Degree

With the successful completion of the course the student acquires the MSc in Biology with the specialization (Major) "Infectious Diseases". The entire master program is designed for four semesters, but can also be completed within three semesters if the lab rotations from the third semester are already completed in the second semester. This Master degree qualifies students to enter PhD programs in Europe or could be a starting

CONTACT POINT

Major Infectious Diseases

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Education at the Department of Infectious Diseases

The Department of Infectious Diseases at the Medical Faculty of Heidelberg represents the subject of Infectious Diseases in research, education and diagnostics, in the fields of bacteriology, virology, parasitology and tropical medicine. There are five units and two sections with a large number of research groups, most of which are involved in the educational activities of this Major. The involved units and sections are:

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

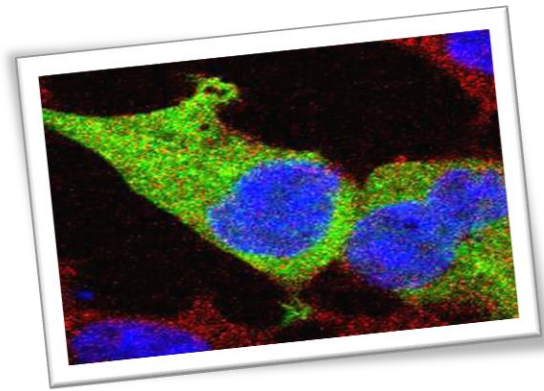


Medical Microbiology and Hygiene

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.

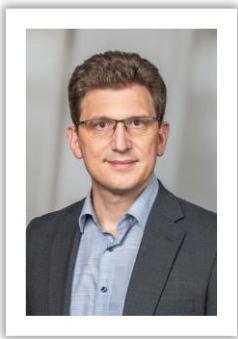


In order to address these topics we are using a multitude of methods and experimental approaches covering the fields of immunology, microbiology, molecular and cell biology as well as biochemistry.

The following teams belong to Medical Microbiology:

- Prof. Dr. med. Alexander Dalpke (Head of the Medical Microbiology)
- Prof. Dr. Stefan Jordan
- Dr. Bachar Cheaib
- Dr. Vivek Thacker

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, 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, 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, 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, Dalpke AH: Bronchial epithelial cells induce alternatively activated dendritic cells dependent on glucocorticoid receptor signaling. *J Immunol* **2014**; 193(3): 1475-84

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

Gehrig S, Eberle ME, Botschen F, Rimbach K, Eberle F, Eigenbrod T, Kaiser S, Holmes WM, Erdmann VA, Sprinzel M, Bec G, Keith G, Dalpke AH*, 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, Dalpke AH: Suppressor of cytokine signaling 1 (SOCS1) limits NFκB signaling by decreasing p65 stability within the cell nucleus. *FASEB J* **2011**; 25(3): 863-874

Schmidt LM, Belvisi MG, Bode KA, Bauer J, Schmidt C, Suchy MT, Tsikas D, Scheuerer J, Lasitschka F, Gröne HJ, 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, 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, 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

Prof. Dr. Stefan Jordan



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Scientific Vita

Since 2024: Professor for Host – Microbiome Interactions, Dept. of Infectious Diseases, University Hospital Heidelberg

2019-2024: Independent group leader, Institute of Microbiology, Infectious Diseases and Immunology, Charité – Universitätsmedizin Berlin, Germany

2018-2019: Associate Scientist, Precision Immunology Institute, Icahn School of Medicine at Mount Sinai, New York, USA

2013-2018: Postdoctoral fellow, Icahn School of Medicine at Mount Sinai, New York, USA

2012-2013: Postdoctoral fellow, Max von Pettenkofer-Institute and Gene Center, Ludwig-Maximilians-University Munich, Germany

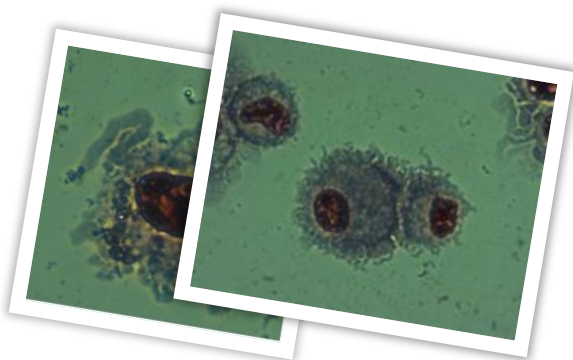
2007-2011: Doctorate, Max von Pettenkofer-Institute and Gene Center, Ludwig-Maximilians-University Munich, Germany

2000-2006: Studies of Biochemistry, Leipzig University, Universidad de Granada, Technical University of Munich (TUM)

1999-2000: General studies, Leibniz Kolleg, Tübingen, Germany

Specific Research Interests

- We investigate the molecular and cellular mechanisms by which dietary intake affects the microbiome and the immune system. Our focus is on the anti-inflammatory and anti-aging effects of caloric restriction and fasting. To this aim, we use laboratory mice with a natural microbiome as well as analyze samples from clinical trials.



Selected Publications

(complete list ORCID ID 0000-0001-9330-1715)

Delconte RB, Owyong M, Santosa EK, Srpan K, Sheppard S, McGuire TJ, Abbasi A, Diaz-Salazar C, Chun J, Rogalsky I, Hsu KC, Jordan S, Merad M, Sun J: Fasting reshapes tissue-specific niches to improve NK cell-mediated anti-tumor immunity. *Immunity* **2024**; 57(8):1923-1938

Jordan S+, Tung N, Casanova-Acebes M, Chang C, Cantoni C, Zhang D, Wirtz TH, Naik S, Rose SA, Brocker CN, Gainullina A, Hornburg D, Horng S, Meier BB, Cravedi P, LeRoith D, Gonzalez FJ, Meissner F, Ochando J, Rahman A, Chipuk JE, Artyomov MN, Frenette PS, Piccio L, Berres M-L, Gallagher EJ, Merad M+: Dietary intake regulates the circulating inflammatory monocyte pool. *Cell* **2019**; 178(5):1102-1114

Dr. Bachar Cheaib



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Scientific Vita

2023-present: Group Leader, Department of Infectious Diseases, Medical Microbiology and Hygiene, Heidelberg University hospital

2018-2023: Post-doctoral Research Associate at the University of Glasgow, Scotland, United Kingdom

2013-2018: Ph. D Institute de Biologie Intégrative et des Systèmes, Université Laval, Québec City, Canada

Specific Research Interests

- Eco-evolutionary basis of host-microbiome colonisation
- Evolutionary medicine and microbial evolution of antimicrobial resistance
- Microbiome Dynamics and ontogenesis of respiratory and digestive tracts
- Host-microbe spatial Omics to reveal the cell-cell communication in the context of infection
- Molecular microbe-microbe interactions from function redundancy to metabolic cross-feeding

Selected Publications

Quintana JF, Sinton MC, Chandrasegaran P, Lestari AL, Heslop R, Cheaib B, et al.: $\gamma\delta$ T cells control murine skin inflammation and subcutaneous adipose wasting during chronic *Trypanosoma brucei* infection. **Nat Commun** 2023; 14(1):5279

Cheaib B, et al.: Genome erosion and evidence for an intracellular niche – exploring the biology of mycoplasmas in Atlantic salmon. **Aquaculture** 2021; 541:736772

Kazlauskaitė R, Cheaib B, Heys C, et al.: SalmoSim: the development of a three-compartment in vitro simulator of the Atlantic salmon GI tract and associated microbial communities. **Microbiome** 2012; 9(1):179

Cheaib B, Seghouani H, Llewellyn M, et al.: The yellow perch (*Perca flavescens*) microbiome revealed resistance to colonisation mostly associated with neutralism driven by rare taxa under cadmium disturbance. **Anim Microbiome** 2021; 3(1):3

Cheaib B, Seghouani H, Ijaz UZ, Derome N: Community recovery dynamics in yellow perch microbiome after gradual and constant metallic perturbations. **Microbiome** 2020; 8(1):14

Cheaib B, Heys C, Busetti A, Kazlauskaitė R, Maier L, Sloan W, Ijaz UZ, Kaufmann J, McGinnity P, Llewellyn L: Neutral processes dominate microbial community assembly in Atlantic salmon, *Salmo salar*. **Appl Environ Microbiol** 2020; 86(8):e02283-19

Cheaib B, Le Boulch M, Mercier PL, Brochu F, Derome N: Taxon-Function Decoupling as an Adaptive Signature of Lake Microbial Metacommunities Under a Chronic Polymetallic Pollution Gradient. **Front Microbiol** 2018; 9:

Dr. Vivek Thacker



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infektiologie/medizinische-mikrobiologie-und-hygiene/forschung/research/thacker

Scientific Vita

Since 2023: Tenured Group Leader, Department of Infectious Diseases, Heidelberg University Medical Faculty

2021-2023: Senior Scientist, Ecole Polytechnique Fédérale de Lausanne (EPFL), Switzerland

2015-2021: Postdoctoral Fellow, Ecole Polytechnique Fédérale de Lausanne (EPFL), Switzerland

2016-2019: Human Frontier Science Program Long-Term Fellow

2014-2015: Postdoctoral Fellow, Department of Physics, University of Cambridge, UK

2010-2014: PhD in Physics, University of Cambridge, UK

2006-2010: BA/MSci in Natural Sciences, Trinity College, University of Cambridge, UK

Specific Research Interests

- Tuberculosis
- COVID-19
- urinary tract infections
- organ-chip and organoid models
- host-pathogen interactions
- innate immunity
- biophysics

Selected Publications

Yin DE, Palin AC, Lombo TB, Mahon RN, Poon B, Wu DY, Atala A, Brooks KM, Chen S, Coyne CB, D'Souza P, Fackler OT, Furler O'Brien RL, Garcia-de-Alba C, Jean-Philippe P, Karn J, Majji S, Muotri AR, Ozulumba T, Sakatis MZ, Schlesinger LS, Singh A, Spiegel HML, Struble E, Sung K, Tagle DA, Thacker VV, Tidball AM, Varthakavi V, Vunjak-Novakovic G, Wagar LE, Yeung CK, Ndhlovu LC, Ott M: 3D Human Tissue Models and Microphysiological Systems for HIV and Related Comorbidities. **Trends Biotechnol** 2024; 42(5), 526-543

Mishra R, Hannebelle M, Patil VP, Dubois A, Garcia-Mouton C, Kirsch G, Jan M, Sharma K, Guex N, Sordet-Dessimoz J, Perez-Gil J, Prakash M, Knott GW, Dhar N, McKinney JD, Thacker VV: Mechanopathology of biofilm-like *M. tuberculosis* cords. **Cell** 2023; 186(23), 5135-5150

Di Domizio J, Gulen MF, Saidoune F, Thacker VV, Yatim A, Sharma K, Guenova E, Schaller M, Conrad C, Göpfert C, De Leval L, von Garnier C, Berezowska S, Dubois A, Gilliet M, Ablasser A: The cGAS-STING pathway drives type I IFN immunopathology in COVID-19. **Nature** 2022; 603, 145-151

Thacker VV, Sharma K, Dhar N, Mancini G, Sordet-Dessimoz J, McKinney JD: Rapid endotheliitis and vascular damage characterize SARS-CoV-2 infection in

a human lung-on-chip model. **EMBO Reports** 2021; 22: e52744

Sharma K, Thacker VV, Dhar N, Signorino-Gelo F, Clapés Cabrer M, Dubois A, Mullenders J, Knott G, Clevers H, McKinney JD: Early invasion of the bladder wall by solitary bacteria protects uropathogenic *E. coli* from antibiotics and neutrophil swarms in an organoid model. **Cell Reports** 2021; 36(3): e109351

Sharma K, Dhar N, Thacker VV, Simonet TM, Signorino-Gelo F, Knott G, McKinney JD: Dynamic persistence of UPEC intracellular bacterial communities in a human bladder-chip model of urinary tract infection. **eLife** 2021; 10: e66481

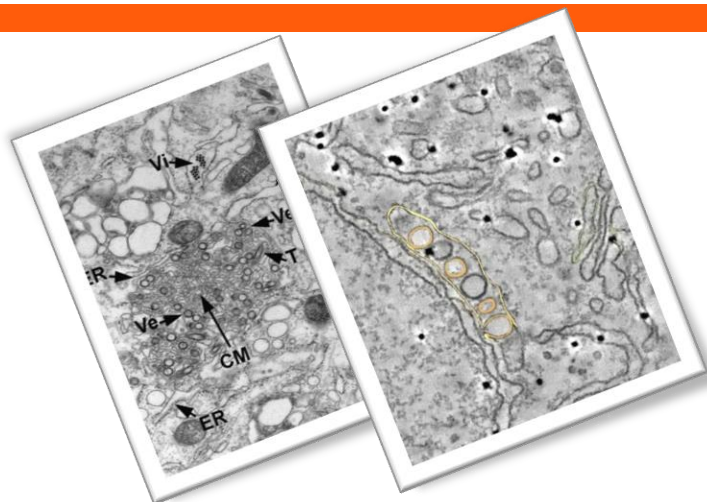
Thacker VV, Dhar N, Sharma K, Barrile R, Karalis K, McKinney JD: A lung-on-chip infection model of early *M. tuberculosis* infection reveals an essential role for alveolar epithelial cells in controlling bacterial growth. **eLife** 2020; 9: e59961

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

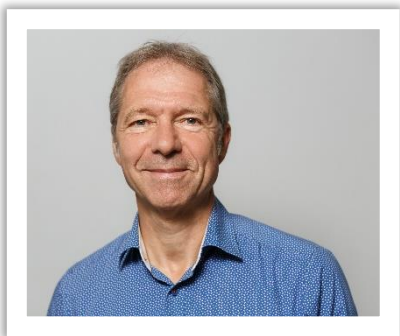


biology, biochemistry and immunology. In addition to state-of-the-art methods in these fields we use live cell imaging, cutting edge light and electron microscopy as well as 3D reconstructions.

The following teams belong to Molecular Virology:

- Prof. Dr. Dr. h.c. 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

Prasad V, Cerikan B, Stahl Y et al. and Bartschlagler R: Enhanced SARS-CoV-2 entry via UPR-dependent AMPK-related kinase NUA2. *Mol Cell* 2023; 83(14):2559-2577, PMID: 37421942

Cortese M, Lee J-Y, Cerikan B et al. and Bartschlagler R: Integrative Imaging Reveals SARS-CoV-2-Induced Reshaping of Subcellular Morphologies. *Cell Host Microbe* 2020; 28(6):853-866, PMID: 33245857

Neufeldt CJ, Cortese M, Scaturro P, Cerikan B, Wideman JG, Tabata K, Moraes T, Oleksiuk O, Pichlmair A, Bartschlagler R: ER-shaping atlastin 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, Börol J, Salzburger W, Kaderali L, Briggs JAG, Bartschlagler 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, Bartschlagler 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, Bartschlagler 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, Bartschlagler 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, Bartschlagler R: Composition and three-dimensional architecture of the dengue virus replication and assembly sites. *Cell Host Microbe* 2009; 5(4): 365-75

Wakita T*, Pietschmann T*, Kato T, Date T, Miyamoto M, Zhao Z, Murthy K, Habermann A, Kräusslich HG, Mizokami M, Bartschlagler R*, Liang TJ: 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, Bartschlagler R: Replication of subgenomic HCV RNAs in a hepatoma cell line. *Science* 1999; 285(5424): 110-3

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

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 direct acting antivirals on HBV and HDV infection for the therapy of liver diseases
- Development of point of care (POC) test for HDV

Selected Publications

Wedemeyer H, Aleman S, Brunetto MR, Blank A, Andreone P, Bogomolov P, Chulanov V, Mamonova N, Geyvandova N, Morozov V, Sagalova O, Stepanova T, Berger A, Manuilov D, Suri V, An Q, Da B, Flaherty J, Osinusi A, Liu Y, Merle U et al. for the MYR 301 Study Group: A Phase 3, Randomized Trial of Bulevirtide in Chronic Hepatitis D. *N Engl J Med* 2023; 389(1): 22-32

Wedemeyer H, Schöneweis K, et al. and Urban S: A multicentre, randomised, parallel-group, open-label phase 2 clinical trial (MYR202) to assess safety and efficacy of bulevirtide in combination with tenofovir disoproxil fumarate in patients with HBV/HDV coinfection. *Lancet Infect Dis* 2022; 23(1):117-129

Zhang Z, Ni Y, Lempp FA, Walter L, Mutz P, Bartschlagler R, 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, 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

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, Filzmayer C, Ni Y, Sültmann H, Mutz P, Hiet MS, Vondran FWR, Bartschlagler 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, Mehre S, Nkongolo S, Kaufman C, Fälth M, Stindt J, Königler C, Nassal M, Kubitz R, 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, Bartschlagler 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, 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

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

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Scientific Vita

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

Tran CS, Kersten J, Yan J, Breinig M, Huth T, Poth T, Colasanti O, Riedl T et al. and Lohmann V: Phosphatidylinositol 4-Kinase III Alpha Governs Cytoskeletal Organization for Invasiveness of Liver Cancer Cells. *Gastroenterology* 2024; 167(3):522-537

Colasanti O, Burm R, Huang H, Riedl T, Traut J, Gillich N, Li T-F, Corneillie L, Faure-Dupuy S, Grünvogel O, Heide D, Lee J-Y, Tran C S, Merle U, Chironna M, Vondran F F W, Esser-Nobis K, Binder M,

Bartenschlager R, Heikenwälder M, Meuleman P, Lohmann V: Comparison of HAV and HCV infections in vivo and in vitro reveals distinct patterns of innate immune evasion and activation. *J Hepatol* 2023; 579(3):645-656

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

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

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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(10)

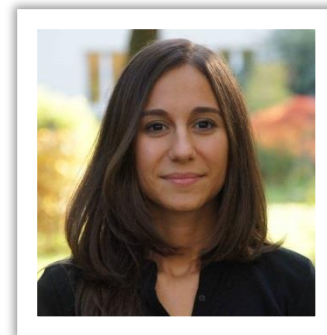
Harak C, Meyrath M, Romero-Brey I, Schenk C, Gondeau C, Schult P, Esser-Nobis K, Saeed M, Neddermann P, Schnitzler P, Gotthardt D, Perez-Del-Pulgar S, Neumann-Haefelin C, Thimme R, Meuleman P, Vondran FW, Francesco R, Rice CM, Bartenschlager R, Lohmann V: Tuning a cellular lipid kinase activity adapts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

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

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

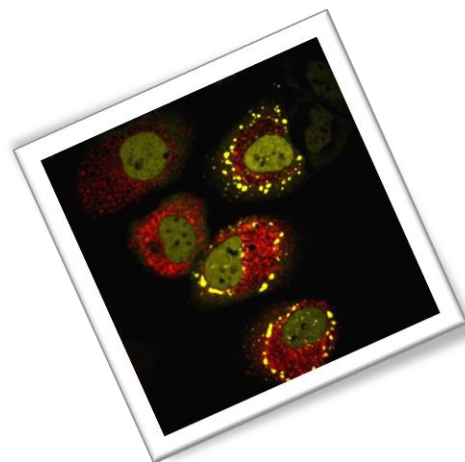
Lohmann V., Körner F, Koch JO, Herian U, Theilmann L, Bartenschlager R.: Replication of subgenomic hepatitis C virus RNAs in a hepatoma cell line. *Science* 1999; 285: 110-113

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Scientific Vita

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

2008–2013: PostDoc at the Department of Infectious Diseases, Heidelberg University

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 α -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.

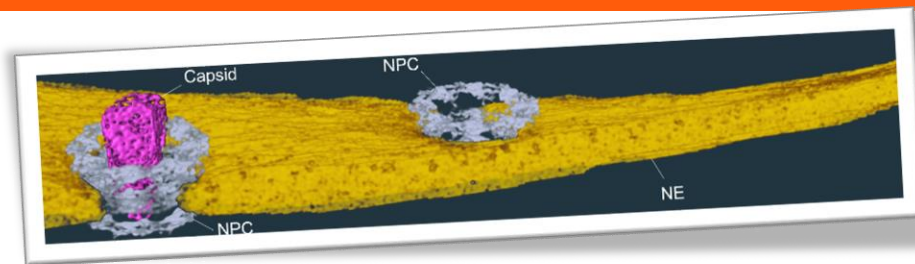
Virology

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.

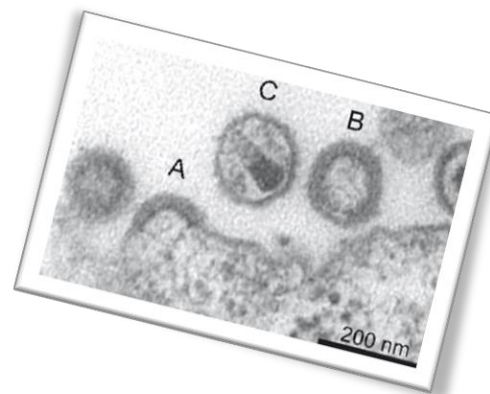
Other viral systems studied include parvoviruses, influenza virus and hepatitis E virus. We develop and use vectors based on adeno-associated virus for basic research and gene therapy approaches (Grimm) and exploit the CRISPR/Cas system for gene therapeutic and antiviral strategies (Grimm, Kräusslich). The 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. Dr. h.c. 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



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Scientific Vita

2019–2023: 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)

Specific Research Interests

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

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

Bejarano DA, Peng K, Laketa V, Börner K, Jost KL, Lucic B, Glass B, Lusic M, Müller B, Kräusslich HG: HIV-1 nuclear import in macrophages is regulated by CPSF6-capsid interactions at the nuclear pore complex. **Elife 2019**; 8:e41800

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

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

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

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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

- Virus-host interactions in the post-entry phase of retroviral replication
- HIV assembly and maturation
- Dynamics of HIV cell entry and HIV particle formation
- Fluorescently labeled virus derivatives

Selected Publications

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**

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 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

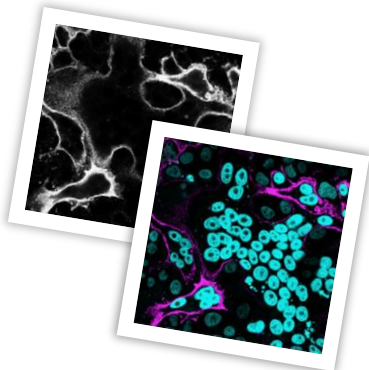
Pape C, Remme R, Wolny A, Olberg S, Wolf S, Cerrone L, Cortese M, Klaus S, Lucic M, Ullrich S, Wolf S, Cerikan B, Neufeldt CJ, Ganter M, Schnitzler P, Merle U, Lusic M, Boulant S, Stanifer M, Bartenschlager R, Hamprecht FA, Kreshuk A, Tischer C, Kräusslich HG, Müller B, Laketa V: Microscopy-based assay 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, Pachel P, Sacha P, Cigler P, Weber J, Majer P, Rezacova P, Kräusslich HG, Müller B***, Konvalinka J***: Triggering HIV polyprotein processing inside virions by rapid photodegradation of a tight-binding photodegradable protease inhibitor. **Nature Communications 2015**; 6:6461

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



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Scientific Vita

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

Selected Publications

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, Touelle M, Ronzitti G, Hebben M, Mingozi 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; 8(38):eabn4704

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, Stüllein C, Fakhiri J, Zimmermann 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, Niopek 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, Stücker 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, 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, 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, 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, Kay MA: Fatality in mice due to oversaturation of cellular microRNA/short hairpin RNA pathways. **Nature** 2006; 441:537-41

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Scientific Vita

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

Chi H, Ou B, Prawira A, Richardt T, Maurer L, Hu JG, Fu R, Lempp FA, Zhang Z, Grimm D, Wu X, Urban S, Dao Thi VL: Human pluripotent stem cell-derived hepatocyte-like cells for hepatitis D virus studies. **EMBO Rep**, in press

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. **Hepato Comm** 2021; 6(4):878-888

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, Singarja 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

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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

- Structural virology of viral infection
- Cryo-electron tomography, correlative light and electron microscopy
- Membranes
- Influenza A virus, SARS-CoV-2, Ebola virus

Selected Publications

Zimmermann L, Chlanda P: Cryo-electron tomography of viral infection - from applications to biosafety. **Curr Opin Virol** 2023, PMID: 37348443

Bodmer BS, Vallbracht M, Ushakov DS, Wendt L, Chlanda P, Hoenen T: Ebola virus inclusion bodies are liquid organelles whose formation is facilitated by nucleoprotein oligomerization. **Emerg Microbes Infect** 2023, 12(2):2223727, PMID: 37306660

Winter SL, Golani G, Lolicato F, Vallbracht M, Thiagarajah K, Ahmed SS, Lüchtenborg C, Fackler OT, Brügger B, Hoenen T, Nickel W, Schwarz US, Chlanda P: The Ebola virus VP40 matrix layer undergoes endosomal disassembly essential for membrane fusion. **EMBO J** 2023, 42(11):e113578, PMID: 37082863

Klein S, Golani G, Lolicato F, Lahr C, Beyer D, Herrmann A, Wachsmuth-Melm M, Reddmann N, Brecht R,

Hosseinzadeh M, Kolovou A, Makroczyova J, Peterl S, Schorb M, Schwab Y, Brügger B, Nickel W, Schwarz US, Chlanda P: IFITM3 blocks influenza virus entry by sorting lipids and stabilizing hemifusion. **Cell Host Microbe** 2023, 12;31(4):616-633.e20, PMID: 37003257

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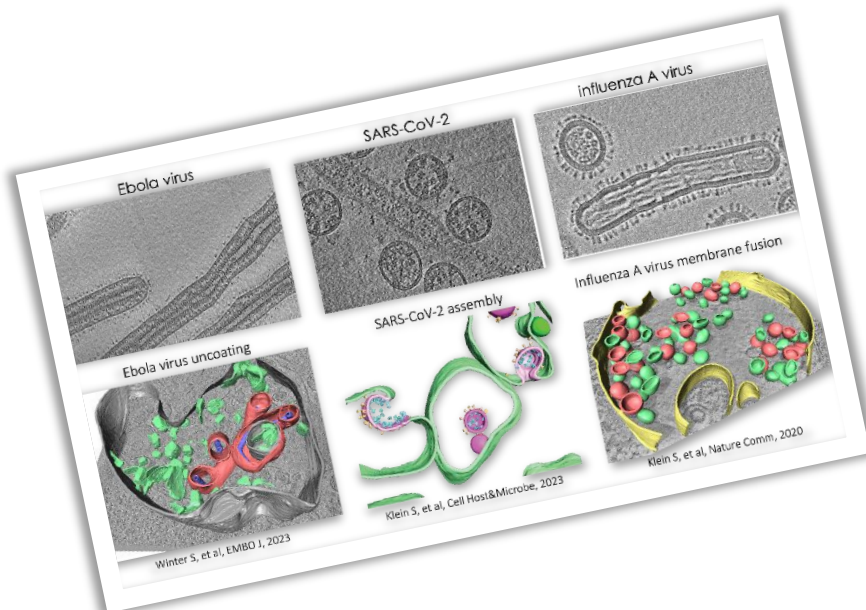
Winter SL, Chlanda P: Dual-axis Volta phase plate cryo-electron tomography of Ebola virus-like particles reveals actin-VP40 interactions. **J Struct Biol** 2021, 213(2):107742, PMID: 33971285

Klein S, Wimmer BH, Winter SL, Kolovou A, Laketa V, Chlanda P: Post-correlation on-lamella cryo-CLEM reveals the membrane architecture of lamellar bodies. **Commun Biol** 2021, 4(1):137, PMID: 33514845

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Klein S, Müller TG, Khalid D, Sonntag-Buck V, Heuser AM, Glass B, Meurer M, Morales I, Schillak A, Freistaedter A, Ambiel I, Winter SL, Zimmermann L, Naumoska T, Bubeck F, Kirrmaier D, Ullrich S, Barreto Miranda I, Anders S, Grimm D, Schnitzler P, Knop M, Kräusslich HG, Dao Thi VL, Börner K, Chlanda P: SARS-CoV-2 RNA Extraction Using Magnetic Beads for Rapid Large-Scale Testing by RT-qPCR and RT-LAMP. **Viruses** 2020, 12(8):863, PMID: 32784757

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, 1(6):16050



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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, Heidelberg University

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

2008-2011: BSc (Biological Science), 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, Goldber I, Burns A, Mavin 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, Oliveira 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, Oliveria 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

Wang Z*, Muecksch F*, Schaefer-Babajew D*, Finkin S*, Viant C*, Gaebler C*, Hoffmann H-H, Barnes CO, Cipolla C, Ramos V, Oliveira TY, Cho A, Schmidt F, da

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*, CLorenzi JC*, Wang Z*, Cho A*, Agudelo M*, Barnes CO*, Gazumyan A*, Finkin S*, Hägglöf 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, Hartweg 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

Mücksch F*, Citir M*, Lüchtenborg C, Glass B, Traynor-Kaplan A, Schultz C, Brügger B, Kräusslich HG: Quantification of phosphoinositides reveals strong enrichment of PIP₂ in HIV-1 compared to producer cell membranes. **Sci Rep** 2019; 9, 17661

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

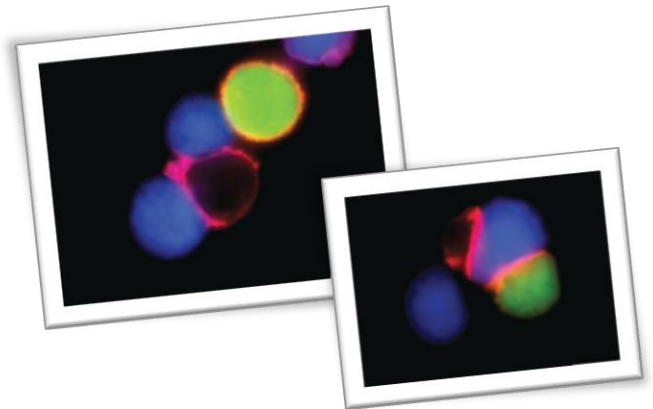
While an overall goal of our laboratory is to explore the specific contributions of nuclear topology and chromatin factors to HIV integration site selection and establishment of latency, we are specifically interested in determining the role of nuclear pore complex proteins in integration site selection.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



Prof. Dr. Oliver T. Fackler



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Scientific Vita

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

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

2003: Habilitation in experimental virology, Heidelberg University

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

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

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

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

1989-1993: Studies in biology (Saarbrücken)

Specific Research Interests

- Immuno- and cell biology of HIV infection
- 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

Morath K, Sadhu L, Dyckhoff G, Gapp M, Keppler OT, Fackler OT: Activation-Neutral Gene Editing of CD4 T cells in Human ex Vivo Tonsil Cultures. **Cell Rep Meth** 2024; 4, 100685

Ananth S, Ambiel I, Schifferdecker S, Müller TG, Wrtil PR, Mejias-Perez E, Kräusslich HG, Müller B, Keppler OT, Fackler OT: Spatial resolution of HIV-1 post-entry steps in resting CD4 T cells. **Cell Rep** 2024; 43, 113941

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Gallucci L, Abele T, Fronza R, Stolp B, Laketa V, Sid Ahmed S, Flemming A, Müller B, Göpflich K, Fackler OT: Tissue-like Environments Shape Functional Interactions of HIV-1 with Immature Dendritic Cells. **Embo Rep** 2023; 24:e56818

Sadhu L, Tsopolidis N, Hasanuzzaman H, Laketa V, Way M, Fackler OT: ARPC5 Isoforms and Their Regulation by Calcium-Calmodulin-N-WASP Drive Distinct Arp2/3-dependent Actin Remodeling Events in CD4 T Cells. **eLife** 2023; 12:e82450

Kaw S, Ananth S, Tsopolidis N, Morath K, Coban BM, Hohenberger R, Bulut OC, Klein F, Stolp B, Fackler OT: HIV-1 infection of CD4 T cells impairs antigen-specific B cell function. **EMBO J** 2020; 39: e105594

Imle A, Kumberger P, Schnellbacher 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

Tsopolidis 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

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

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)

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Scientific Vita

2014-present: Group Leader, Center of Infectious Diseases, Integrative Virology, Heidelberg University Hospital. Tenure Track Professor for Preclinical HIV-1 Research

2008-2013: Research scientist and project leader in Molecular Medicine Laboratory, ICGEB, Trieste; Extended faculty member, San Raffaele Scientific Institute, Milan

2004-2008: Post-doctoral scientist in Molecular Medicine lab, ICGEB, Trieste

1999-2003: PhD student (ICGEB Fellowship) in Molecular Medicine Laboratory, International Centre for Genetic Engineering and Biotechnology (ICGEB), Trieste, Italy. PhD degree in Molecular Biology and Biochemistry, Faculty of Biological Sciences, University of Belgrade

Specific Research Interests

- Nuclear organization and chromatin landscape in viral infection
- Blood and brain immune cells as HIV-1 reservoirs (CD4 T cells and microglia)
- R-loops and mRNA splicing helicase complex in HIV-1 integration
- Metabolism and epigenetics in viral infection

Selected Publications

Rheinberger M, Costa AL, Kampmann M, Glavas D, Shytaj L, Penzo C, Tibroni N, Fackler O, Vlahovick K, Lusic B, Herrmann C, Lusic M: Genomic profiling of HIV-1 integration in microglia cells links viral integration to the topologically associated domains. **Cell Reports** 2023; 13;42(2):112110

Shytaj IL, Fares M, Lusic B, Galluci L, Tolba M, Zimmermann L, Ayoub AT, Cortese M, Neufeldt CJ, Laketa V, Chlanda P, Fackler OT, Boulant S, Bartenschlager R, Stanifer M, Savarino A, Lusic M: The FDA-approved drug cobicistat synergizes with remdesivir to inhibit SARS-CoV-2 replication in vitro and decreases viral titers and disease progression in Syrian hamsters. **mBio** 2022; 1:13(2)

Lusic B, de Castro IJ, Lusic M: Viruses in the Nucleus. **Cold Spring Harb Perspect Biol** 2021; 13(8):a039446

Shytaj IL, Procopio FA, Tarek M, Carlon -Andres I, Tang H-Y, Goldman, AR, Munshi, MH, Forcato M, Leskov K, Ye F, Lusic B, Cruz N, Singh A, Biccato S, Padilla-Parra S, Diaz RS, Lusic M, Karn J, Alvarez-Carbonell D, Savarino A: Glycolysis downregulation is a hallmark of HIV-1 latency and sensitizes infected cells to oxidative stress. **EMBO Mol Med** 2021; 13(8):e13901

Zila V, Margiotta E, Turonova B, Müller TG, Zimmerli C, Mattei S, Allegretti M, Borner K, Rada J, Müller B, Lusic M, Kräusslich HG, Beck M: Cone-shaped HIV-1 Capsids are transported through intact nuclear pores. **Cell** 2021; 184, 1-15

Shytaj IL, Lusic B, Forcato M, Penzo, C, Billingsley J, Laketa V, Bosinger S, Stanic M, Gregoretti F, Antonelli L, Oliva G, Frese K, Trifunovic A, Galy B, Eibl C, Silvestri G, Biccato S, Savarino A, Lusic M: Alterations of redox and iron metabolism accompany development of HIV latency. **EMBO J** 2020; 39(9)

Lusic B, Chen H-C, Kuzman M, Zorita E, Wegner J, Minneker V, Wang W, Fronza R, Laufs S, Schmidt M, Stadhouders R, Roukos V, Vlahovick K, Filion GJ, Lusic M: Spatially clustered loci with multiple enhancers are frequent targets of HIV-1. **Nature Commun** 2019; 10(1):4059

Michieletto D, Lusic M, Orlandini E, Marenduzzo D: Physical principles of retroviral integration. **Nat Commun** 2019; 10(1):575

Lusic M, Robert F. Siliciano: Nuclear landscape of HIV-1 infection and integration. **Nat Rev Microb** 2017; 15(2):69-82

Marini B, Kertesz-Farkas A, Lusic B, Hashim A, Lisek K, Manganaro L, Pongor S, Luzzati R, Mavilio F, Giacca M, Lusic M: Nuclear architecture dictates HIV-1 integration site selection. **Nature** 2015; 14; 521(7551):227-31

Parasitology

Fields of Interest

Malaria has remained one of the most important infectious diseases worldwide, causing an estimated 249 million clinical cases and killing approximately 608,000 people every year (World Malaria Report, 2023). 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.

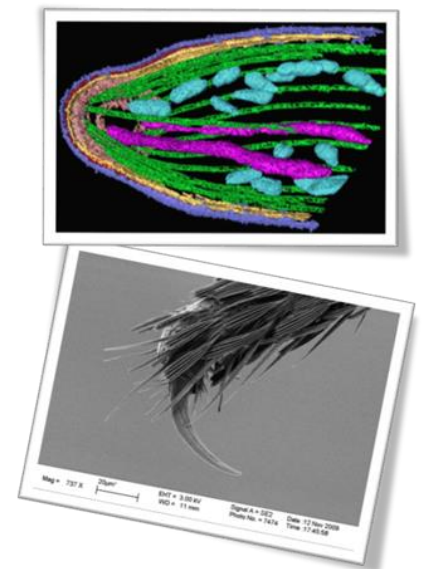
The Thomson-Luque lab (MCTU) focuses on the development of novel anti-malaria vaccines and therapies. We are funded by Sumaya-Biotech, and are currently testing a malaria vaccine based on the fIMSP-1 protein which targets both liver and blood stages of the malaria parasite *Plasmodium falciparum*. After 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 SwisTPH 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 Hentzschel lab investigates the sexual replication of *Plasmodium* parasites in the mosquito. Here, within only 15 minutes eight male gametes form from a single precursor cell and fertilise females to continue mosquito infection. The group uses a combination of reverse genetics, live cell and fixed imaging techniques, and interactome studies to reveal the molecular basis for how these male gametes form and how they further contribute to parasite development in the mosquito. In addition, they develop novel genetic tools to enable investigation of gene function in the diploid oocyst stages.

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. Richard Thomson Luque
- Dr. Victoria Ingham
- Dr. Franziska Hentzschel



Prof. Dr. Michael Lanzer



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Scientific Vita

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

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

1996: Habilitation in Microbiology, University of Würzburg

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

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

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

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

Specific Research Interests

- Molecular Parasitology
- Drug resistance mechanisms of the malarial parasite
- Antigenic variation, cytoadherence, protein trafficking in *P. falciparum*
- Membrane transport processes

Selected Publications

Berger F, Gomez GM, Sanchez CP, Posch B, Planelles G, Sohraby F, Nunes-Alves A, Lanzer M: pH-dependence of the *Plasmodium falciparum* chloroquine resistance transporter is linked to the transport cycle. **Nat Commun** 2023; 14: 4234

Gomez GM, D'Arrigo G, Sanchez CP, Berger F, Wade RC, Lanzer M: PfCRT mutations conferring piperazine resistance in *falciparum* malaria shape the kinetics of

quinoline drug binding and transport. **PLoS Pathog** 2023; 19: e1011436

Haag M, Kehrer J, Sanchez CP, Deponte M, Lanzer M: Physiological jump in erythrocyte redox potential during *Plasmodium falciparum* development occurs independent of the sickle cell trait. **Redox Biol** 2022; 58: 102536

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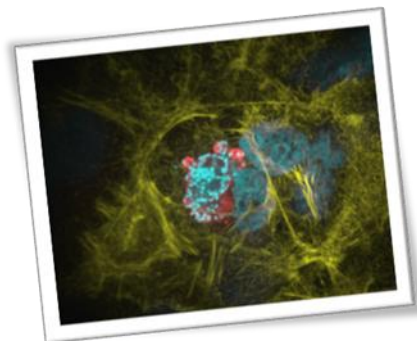
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Sanchez CP, Liu CH, Mayer S, Nurhasanah A, Cyrklaff M, Mu J, Ferdig MT, Stein WD, Lanzer M: A HECT ubiquitin-protein ligase as a novel candidate gene for altered quinine and quinidine responses in *Plasmodium falciparum*. **PLoS Genet** 2014; 10: e1004382

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

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

Lanzer M, de Bruin D, 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

Douglas RG, Moon RW, Frischknecht F: Cytoskeleton Organization in Formation and Motility of Apicomplexan Parasites. **Annu Rev Microbiol** 2024; 39094056

Sattler JM, Keiber L, Abdelrahim A, Zheng X, Jäcklin M, Zechel L, Moreau CA, Steinbrück S, Fischer M, Janse CJ, Hoffmann A, Hentzschel F, Frischknecht F: Experimental vaccination by single dose sporozoite injection of blood-stage attenuated malaria parasites. **EMBO Mol Med** 2024; 39103697

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

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

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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, Frischknecht F: Zinc-finger nuclease-based double strand breaks attenuate malaria parasites and reveal rare micro-homology mediated end joining. **Genome Biology** 2015; 16, 249, 2015

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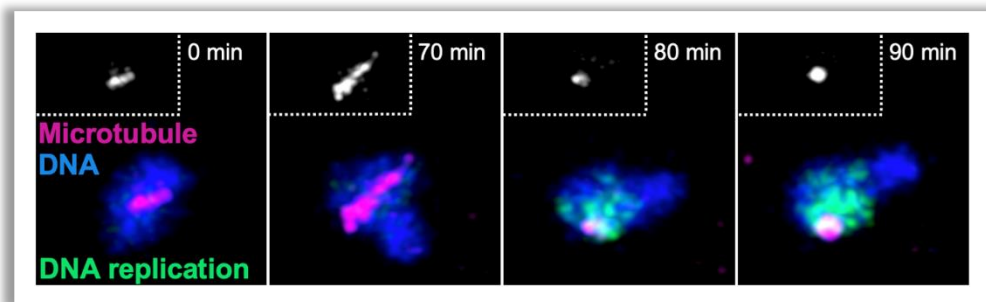
Amino R#, Thiberge S, Martin B, Celli S, Shorte SL, Frischknecht F#, Ménard R#: Quantitative imaging of malaria parasite transmission to the mammalian host. **Nature Medicine** 2006; 12, 220-224

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<https://ciid-heidelberg.de/research-groups/ganter-lab/>



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

Machado M, Klaus S, Klaschka D, Guizetti J, Ganter M: Plasmodium falciparum CRK4 links early mitotic events to the onset of S-phase during schizogony. **mBio** 2023; 14(4):e0077923, PMID: 37345936

Voß Y, Klaus S, Guizetti J, Ganter M: Plasmodium schizogony, a chronology of the parasite's cell cycle in the blood stage. **Plos Pathogens** 2023; 19(3):e1011157, PMID: 36862652

Klaus S, Binder P, Kim J, Machado M, Funaya C, Schaaf V, Klaschka D, Kudulyte A, Cyrklaff M, Laketa V, Hofer 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

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organizes centrosomal microtubules in malaria parasites. **Life Science Alliance** 2021, 4: e202101199, PMID: 34535568

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

Quadt K, Smyrnakou X, Frischknecht F, Böse G, Ganter M: Plasmodium falciparum parasites exit the infected erythrocyte after haemolysis with saponin and streptolysin O. **Parasitology Research** 2020; 119:4297-4302, PMID: 33089360

Ganter M, Goldberg JM, Dvorin JD, Paulo JA, King JG, Tripathi AK, Paul AS, Yang J, Coppens I, Jiang RHY, Baker DA, Dinglasan RR, Gygi SP, Duraisingh MT: Plasmodium falciparum CRK4 directs continuous rounds of DNA replication during schizogony. **Nature Microbiology** 2017; 2, 17017; PMID: 28211852

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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

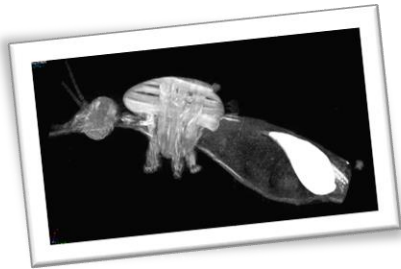
2012-2016: PhD, University of Warwick, UK

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

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

Specific Research Interests

- Vector – parasite interactions in the context of insecticide use
- Molecular mechanisms of insecticide resistance
- Novel active ingredient discovery
- Integration of multiple -omics and molecular biology



Selected Publications

Ingham VA, Grigoraki L, Ranson H: Pyrethroid resistance mechanisms in the major malaria vector species complex. **Entomologia Generalis** 2023; 10.1127/entomologia/2023/1880

Ingham VA et al.: Integration of whole genome sequencing and transcriptomics reveals a complex picture of the reestablishment of insecticide resistance in the major malaria vector *Anopheles coluzzii*. **PLoS Genetics** 2021; 17(12):e1009970

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

Ingham VA, Brown F, Ranson H: Transcriptomic analysis reveals pronounced changes in gene expression due to sublethal pyrethroid exposure and ageing in insecticide resistance *Anopheles coluzzii*. **BMC Genomics** 2021; 22:337

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, 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

Ingham VA, Jones CM, Pignatelli P, Balabanidou V, John Vontas, Wagstaff SC, Moore JD, Ranson H: Dissecting the organ specificity of insecticide resistance candidates in *Anopheles gambiae*: known and novel candidate genes. **BMC Genomics** 2014; 25;15(1):1018

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Web: <https://www.klinikum.uni-heidelberg.de/zentrum-fuer-infektiologie/parasitologie-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 Health Tampa, 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 Triás 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, 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, 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, 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, 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, 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, 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

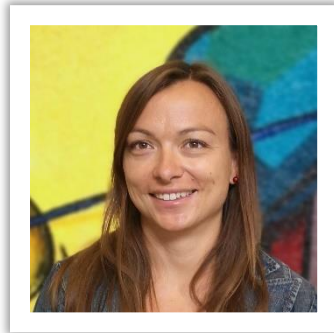
Ntumngia FB, Pires CV, Barnes SJ, George MT, Thomson-Luque R, Kano FS, Alves JRS, Urusova D, Pereira DB, Tolia NH, King CL, Carvalho LH, Adams JH: An engineered vaccine of the *Plasmodium vivax* Duffy binding protein enhances induction of broadly neutralizing antibodies. **Sci Rep** 2017; 7(1):13779

Thomson-Luque R, Saliba KS, Kocken CH, 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, 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, Duraisingh MT, Adams JH, 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

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Scientific Vita

2023-present: Junior group leader, Center of Infectious Diseases, Parasitology, Heidelberg University Hospital, Germany

2021-2023: Postdoc, Center of Infectious Diseases, Parasitology, Heidelberg University Hospital, Germany

2017-2021: Postdoc, Wellcome Center for Integrative Parasitology, University of Glasgow, UK

2013-2017: PhD, University of Heidelberg, Germany

2010-2012: Studies of Molecular Biosciences, Major Infectious Diseases, Heidelberg University, Germany

2007-2010: Studies of Biochemistry, Technical University of Munich, Germany

Specific Research Interests

- Molecular parasitology
- Cell biology of the malaria parasite in the mosquito
- Unusual mitotic replication modes
- Development of novel genetic tools
- Quantitative imaging and single-cell transcriptomics

Selected Publications

Sattler JM, Keiber L, Abdelrahim A, Zheng X, Jäcklin M, Zechel L, Moreau CA, Steinbrück S,

Fischer M, Janse CJ, Hoffmann A, Hentzschel F, Frischknecht F: Experimental vaccination by single dose sporozoite injection of blood-stage attenuated malaria parasites. **EMBO Mol Med** 2024; 16(9):2060-2079

Hentzschel F, Binder AM, Dorner LP, Herzel L, Nuglish F, Sema M, Aguirre-Botero MC, Cyrklaff M, Funaya C, Frischknecht F: Microtubule inner proteins of *Plasmodium* are essential for transmission of malaria parasites. **BioRxiv** 2023; doi: <https://doi.org/10.1101/2023.10.19.562943>

Hentzschel F, Jewanski D, Sokolowski Y, Agarwal P, Kraeft A, Hildenbrand K, Dorner LP, Singer M, Frischknecht F, Marti M: A non-canonical Arp2/3 complex is essential for *Plasmodium* DNA segregation and transmission of malaria. **BioRxiv** 2023; doi: <https://doi.org/10.1101/2023.10.25.563799>

Ferreira J L, Pražák V, Vasishtan D, Siggel M, Hentzschel F, Binder A M, Pietsch E, Kosinski J, Frischknecht F, Gilberger T W, Grünewald K: Variable microtubule architecture in the malaria parasite. **Nat Commun** 2023; 14(1), 1216

Hentzschel F, Frischknecht F: Still enigmatic: *Plasmodium* oocysts 125 years after their discovery. **Trends Parasitol** 2022; 38(8), 610–613 (Review)

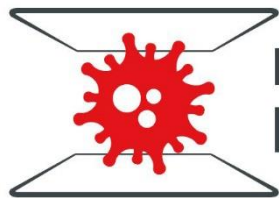
Ripp J, Smyrnakou X, Neuhoﬀ M-T, Hentzschel F, Frischknecht F: Phosphorylation of myosin A regulates gliding motility and is essential for *Plasmodium* transmission. **EMBO Rep** 2022; 23(7):e54857

Hentzschel F, Gibbins M P, Attipa C, Beraldi D, Moxon CA, Otto T D, Marti M: Host cell maturation modulates parasite invasion and sexual differentiation in *Plasmodium berghei*. **Sci Adv** 2022; 8(17):eabm7348

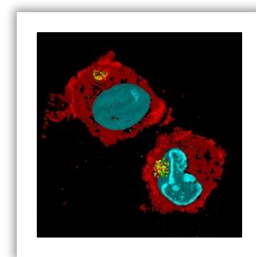
Venugopal K, Hentzschel F, Valkiūnas G, Marti M: *Plasmodium* asexual growth and sexual development in the haematopoietic niche of the host. **Nat Rev Micro** 2020; 18(3), 177–189 (Review)

Hentzschel F, Mitesser V, Fraschka S, Krzikalla D, Carrillo E, Berkhout B, Bártfai R, Mueller A-K, Grimm D: Gene knockdown in malaria parasites via non-canonical RNAi. **Nucleic Acids Res** 2020; 48(1), e2

Hentzschel F, Hammerschmidt-Kemper C, Börner K, Heiss K, Knapp B, Sattler JM, Kaderali L, Castoldi M, Bindman J G, Malato Y, Willenbring H, Mueller A-K, Grimm D: AAV8-mediated in vivo overexpression of miR-155 enhances the protective capacity of genetically-attenuated malarial parasites. **Mol Ther** 2014; 22(12), 2130–214



Infectious Diseases IMAGING PLATFORM



Fields of Interest

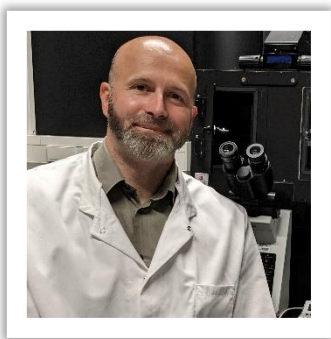
The physiology of host-pathogen interactions is governed by individual, stochastic and often rare molecular events. For example, latent HIV infections occur only in one in a million CD4+ T cells *in vivo*, HCV will only replicate in one out of hundred thousand hepatocyte-derived cells etc. Although, 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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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

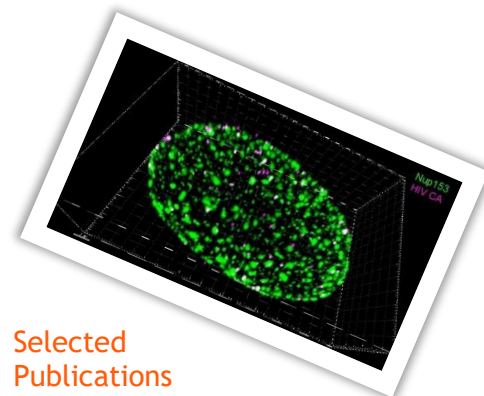
2006-2008 PostDoc, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany

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 patho-physiological 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; 28;18(6):e1010472

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

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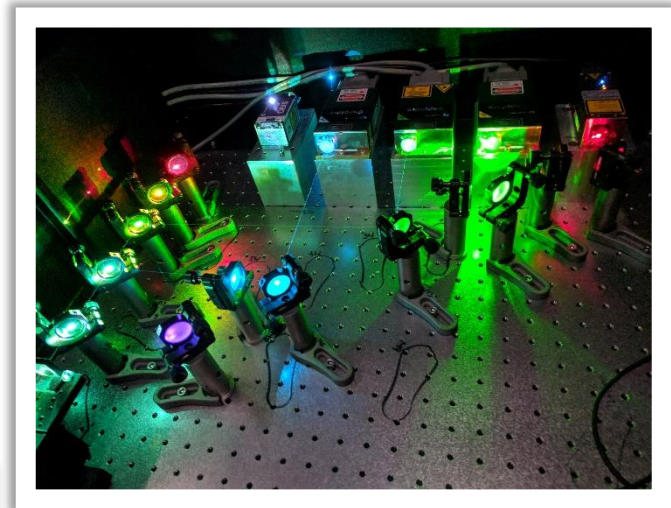
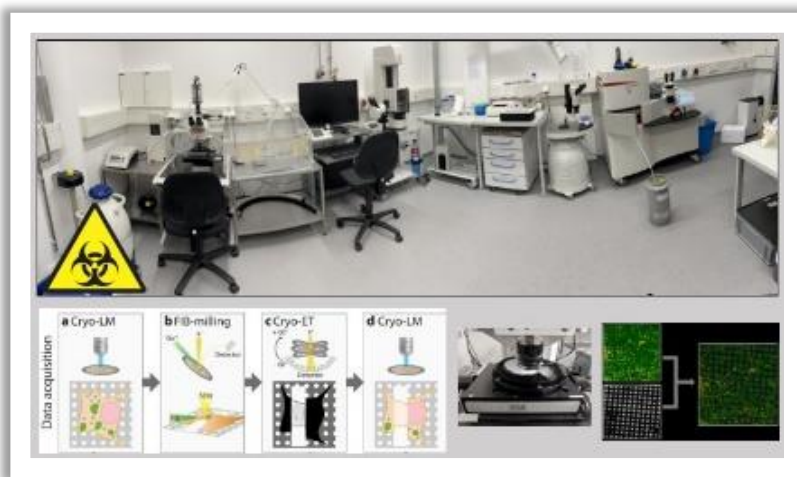
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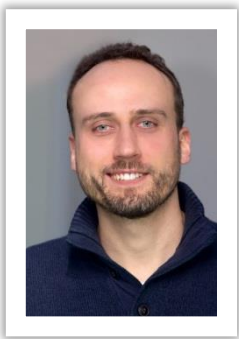
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List of the Associated Research Groups Major Infectious Diseases

German Cancer Research Centre (DKFZ)



Dr. Marco Binder

Research Group "Dynamics of early viral infection and the innate antiviral response"

D430, INF 242; 69120 Heidelberg

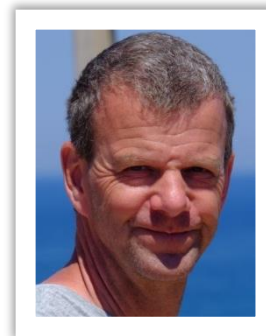
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Email: m.binder@dkfz.de

Web: <https://tinyurl.com/ag-binder>

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
- Interactions of tissue and immune cells



apl. Prof. Dr. Martin Müller

Research Group "Tumorvirus-specific vaccination strategies"

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Web: <http://www.dkfz.de/en/f035/>

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



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



PD Dr. Dr. Angelika Riemer

Division of Immunotherapy and Immunoprevention
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 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



Dr. Erec Stebbins

Research Group "Structural Biology of Infection and Immunity" (D160)
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 Web: <https://www.dkfz.de/en/strukturbiologie-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. Stella E. Autenrieth

Research Group "Dendritic Cells in Infection and Cancer"
 DKFZ, D431, INF 280, 69120 Heidelberg
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 Email: stella.autenrieth@dkfz.de
 Web: <https://www.dkfz.de/en/virus-assoziierte-karzinogenese/groups/AGAutenrieth/index.html?m=1656929068&>

Specific Research Interests

- Immunobiology of dendritic cells (DCs)
- DC development in the context of infection and cancer
- Spectral flow cytometry and unsupervised data analysis
- Immunophenotyping in clinical trials



Prof. Dr. Hedda Wardemann

Research Group "B Cell Immunology / B-Zell-Immunologie" (D130)
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Web: <https://www.dkfz.de/en/b-zell-immunologie/index.php>

Specific Research Interests

- Human immune responses against *Plasmodium falciparum* and SARS-CoV-2
- Malaria vaccine development
- Immunological memory to infection and vaccination
- Antigen-receptor diversity and quality of immune responses

Mannheim Institute for Innate Immunoscience



Prof. Dr. Adelheid Cerwenka

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

Institute of Immunology



Prof. Dr. Yvonne Samstag

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 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, www.cimresearch.org)
- High resolution imaging, InFlow microscopy



PD Dr. Guido Wabnitz

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Specific Research Interests

- Neutrophil heterogeneity: Regulation of Neutrophil Populations
- Neutrophil function in inflammation and inflammatory diseases
- Inter-Leukocyte Communication

Nephrology



PD Dr. Ellen Krautkrämer

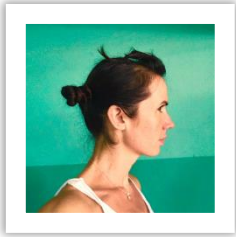
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Web: <http://nierenzentrum-heidelberg.com>

Specific Research Interests

- Replication cycle of hantaviruses in renal cells
- Clinical characteristics of hantavirus infection
- Mechanisms of hantavirus-induced cellular damage and renal failure

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!

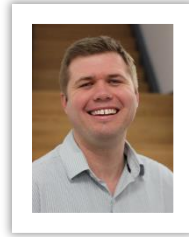


Dr. Silvia Portugal

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Charitéplatz 1; Campus Charité Mitte
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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



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Specific Research Interests

- *Plasmodium* cytoskeleton dynamics



Dr. Pierre-Yves Lozach

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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

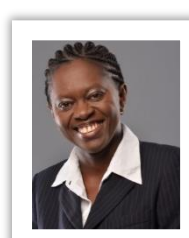


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Specific Research Interests

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



Prof. Dr. Faith Osier

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369 Fulham Road, London SW10 9NH, UK
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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

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Department of Molecular Genetics and Microbiology
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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

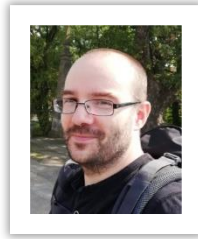


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Specific Research Interests

- 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

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Universität zu Lübeck
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Web: tba

Specific Research Interests

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



Prof. Dr. Dr. Christine E. Engeland

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Specific Research Interests

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

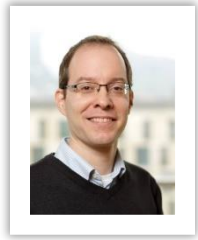


Prof. Dr. med. Dennis Nurjadi

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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



Prof. Dr. Frederik Graw

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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

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



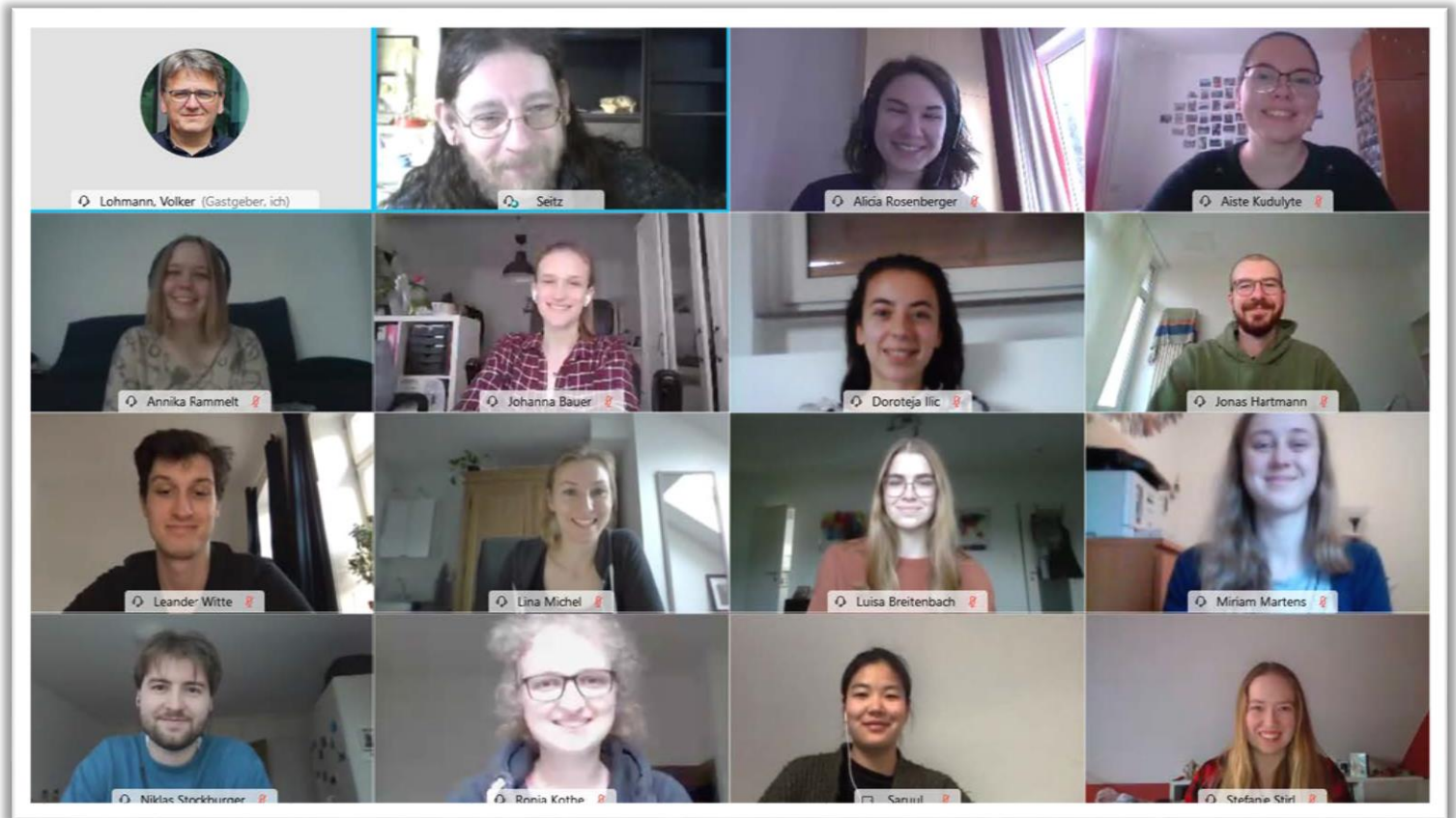
From left to right, in the back: Stefan Diehl, Nikolay Sergeev, Valerii Martynov, Noah Ruf, Jose Luis Guzman Martin, Felix Pahmeier. In the front: Chia Ching Wu, Hao-En Huang, Dorothee Reuß, Laura Emig, Lisa Augstein, Carmen Lahr, Marta Freixas Teres

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.

Students of the Major 'Infectious Diseases' WS 2022-2023



From left to right, in the back: Roberta Malamud, Lena Müller, Marie Rose Schrimpf, Jens Timmer, Lilian Patrick Dorner. In the front: Cheyenne Seeger, Li-Yao Chen, Carla Siebenkotten, Colin Philip Förster, Michelle Georgi, Niclas Maier.

Students of the Major 'Infectious Diseases' WS 2023-2024



From left to right, in the back: Clemens Mathes, Hannah Simonis, Sanya Middha, Kolja Hildenbrand, Yllka Kabashi, Muriel Lauer, Lottida Phondeth, Richard Langi. In the front: Björn Schwortschik, Lena Tomaschko, Katharina Schaper, Veronika Dempf, Melissa Klein, Christopher Hub, Alejandro Vanazzi.

Students of the Major 'Infectious Diseases' WS 2024-2025



From left to right, in the back: Sarah Upwood, Aiden Hiller, Louisa Marie Schön, Emre Güngör, Alisa Victoria Botsch, Daria Ostaszewska. In the front: Margaux Laresse, Magdalena Urlaub, Johanna Simon, Celina Marie Ronge, Natalia Tsironi, Rebecca Haines.