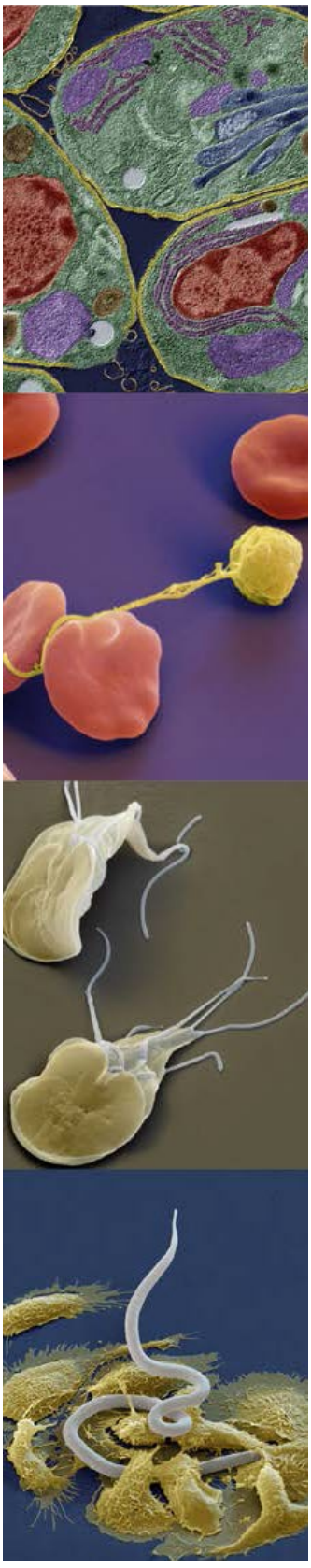
GRK 2046 Newsletter
June 2021



Summary, Update and News

Please enjoy the 11th edition of our biannual GRK 2046 newsletter. As usual, we report from workshops, seminars / lectures, publications and more.
Due to the pandemic, all seminars, talks, workshops and conferences are still available ONLINE only via video conferences. However, we hope that end of 2021 we can test some events to go in person again, talking about the retreat and BPS / Role Models in Infection Biology.

– Marko

New Students

Here you are, a whole bunch of new highly motivated (3rd generation) GRK 2046 PhD students. All started in April, May or June 2021. However, 2 PhD students will start in August. So, we don't have any vacant positions anymore.

Jost Lühle (Project A3, MPICI)

My name is Jost and I joined the Research Training Group in April 2021. I completed my bachelor degree in life sciences at Potsdam University. After this, I moved to Freie Universität Berlin to do a master degree in biochemistry. Early during my studies, I started to be fascinated by the complexity and functional diversity of glycosylation. For my master thesis, I joined the department of Prof. Seeberger and worked on single-domain antibodies targeting tumor-associated carbohydrate antigens. During my PhD, I will aim to exploit the structural difference of parasitic glycans for the establishment of novel glycan-targeted therapies.

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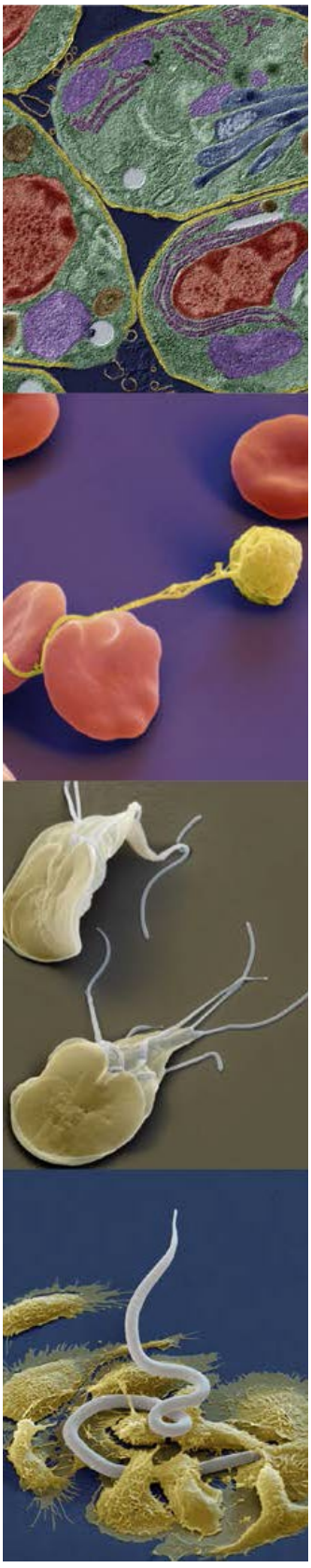

Otto Netzel (Project A6, HUB)

Hello everyone - my name is Otto and I just started my PhD mid April this year. I am originally from the south-west of Germany and did my bachelor's degree in Heidelberg at Friedrich Frischknecht's lab. About three years ago, I switched to Berlin for my master's studies focusing on parasitic infections. I completed my master's at the Institute for Molecular Parasitology working with Alyssa Ingmundson, with whom I now continue to work for my PhD. My project concerns the liver stage of the rodent-specific malaria parasite *Plasmodium berghei*. I want to illuminate mechanisms by which the parasite interacts with the host cell vesicular and endomembrane system to possibly gain access to nutrients and eventually influences the host cell in its favour. In this regard, I am investigating modulation of host Rab-GTPases and their effect on parasite's fitness.

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Luis Elizalde (Project B4, FUB)

Hi all! My name is Luis, I did my Bachelor in Biological Pharmaceutical Chemistry in Mexico. Then, I moved to The Netherlands to obtain my Master degree in Infection & Immunity. Currently, I am a PhD student at the Institute of Immunology working under the supervision of Prof. Dr. Susanne Hartmann. My work focuses on the impact that *Ascaris suum* and *Heligmosomoides polygyrus* infection have on lung immune response. The idea is to decipher how and by which mechanisms are mucosal lung immune cells affected by a strictly enteric nematode (*Heligmosomoides polygyrus*) and by a migrating nematode (*Ascaris suum*).

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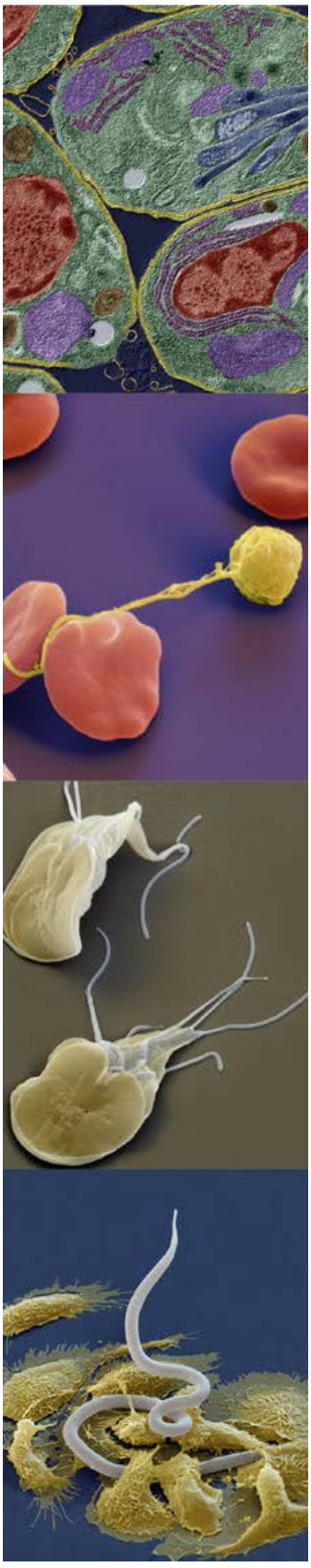

Joshua Adjah (Project B5, FUB)

Hello Everyone! My name is Joshua and I am from Ghana. I completed both my BSc (Biochemistry, Cell and Molecular Biology) and Mphil./MSc (Molecular Cell Biology of Infectious Diseases) at the University of Ghana (Ghana's premier University). After spending most of my student years in malaria research and molecular biology, I decided to move to Germany to pick up a new focus and challenge. I came to Germany in March, 2021 and currently pursing a PhD at the Institute of Immunology of the Freie University in Berlin. My research title is "Genetic, microbial and metabolic profiles associated with resistance to intestinal parasite infections" which seeks to characterize T and B cells kinetics responsible for resistance to helminth infections in mice of different genetic backgrounds.

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Sarah Bala (Project C1, IZW)

My name is Sarah Maria Bala and I am from Germany. I completed my B.Sc. in Biology at the Freie Universität Berlin which was followed by my M.Sc. studies at the Universität Rostock with the focus on Zoology. After the graduation in 2021 I started my PhD at the Institute of Zoo- and Wildlife Research in order to work on apicomplexan parasite load and immune responses in the cheetah.

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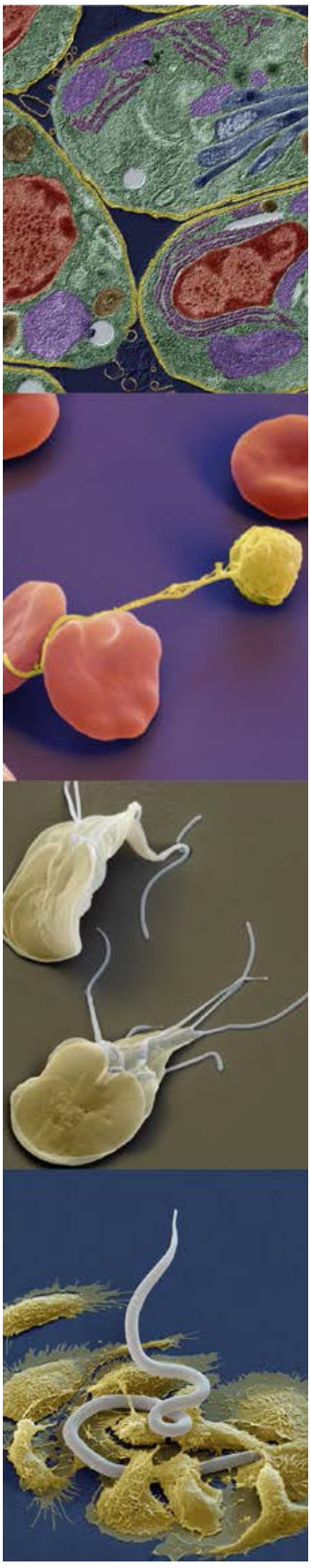

David Warschkau (Project C3, RKI)

I completed both my BSc and MSc degrees in Biochemistry at Freie Universität Berlin. After writing my master thesis at the Max Planck Institute of Colloids and Interfaces, I am now a PhD student at the Robert Koch-Institut in Unit 16: Mycotic and Parasitic agents and Mycobacteria in the group of Prof. Dr. Frank Seeber. In my project, I will use organoids as tools to shed light on the intestinal biology of *Toxoplasma gondii*..

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Susana Soares (Project C4, IZW)

Hi,my name is Susana Soares and I come from Portugal. I completed there my B.Sc. in Basic Animal Health and my MSc in Veterinary Medicine both in the Veterinary Medicine Faculty of the University of Lisbon. Also in my country I finished a post-graduation in Exotic Animals Medicine and Surgery in the University Lusófona in Lisbon. Since then I have been practicing veterinary medicine and giving support in some epidemiology projects in Portugal. In April of 2021 I started a PhD in the Institute for Zoo and Wildlife Research under the GRK2046 program. I will be part of an ongoing project of the Ecological Dynamics department of this institute, within the organismic level of GRAKO, and my PhD will focus on studying determinants of parasite burden and immune responses in a wild social carnivore species - the spotted hyena.

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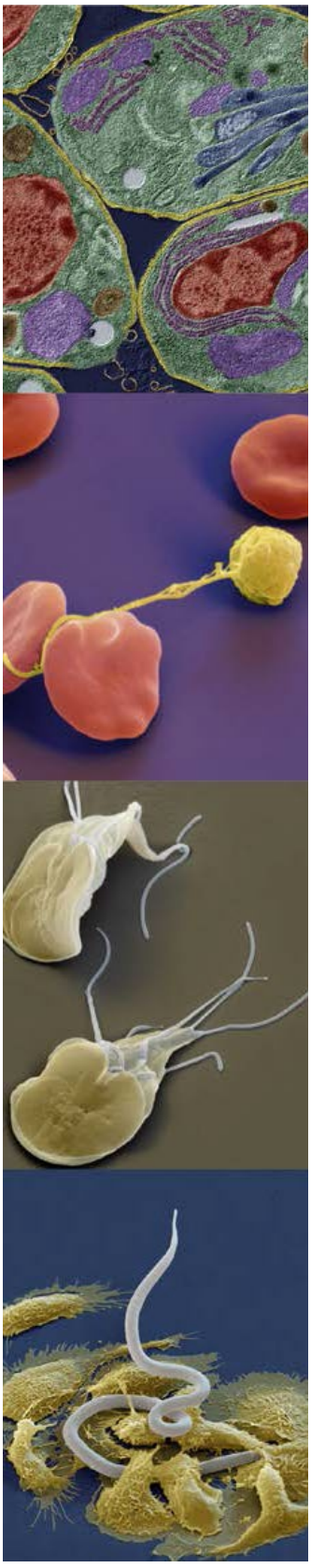

Marly Erazo Lugo (Project C6, MPIIB)

'I am from Colombia and studied Biotechnology at the Technische Universität Berlin. In my master thesis, I worked on the set-up of a simplified human gut microbial consortium. My deep fascination for bacterial interactions motivated me to continue working in the field. In my PhD, I will investigate the impact of environmental microbes on the transmission of *P. falciparum* under the supervision of Elena Levashina at the Max Planck Institute for Infection Biology.

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Megan Peedell (Project C7, CHA)

I graduated from the University of Manchester with a BSc in Biomedical Sciences, before completing a Master of Research degree (MRes) in Infection Biology. My main focus within Infection Biology has been the study of Parasites, namely Plasmodium and Helminths. I started my PhD here in Berlin in April 2021 at the Institute for Tropical Medicine and International Health at the Charité Universitätsmedizin, and my project is investigating the impact of Ascaris-Plasmodium co-infection on antimalarial treatment outcome, re-infection and antimalarial drug resistance.

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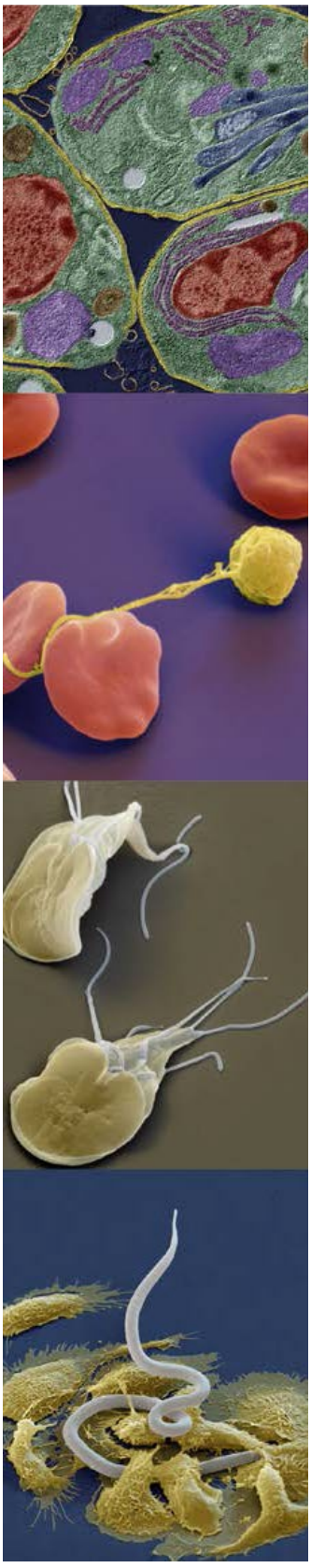

Larissa Oser (Project C9, FUB)

I obtained my title in veterinary medicine after studying in Bern and Berlin. Currently, I am performing my PhD at the institute of immunology at the Freie Universität under the supervision of Prof. Friederike Ebner. My research project aims to investigate the role of antigen-specific T cells in the distribution and predisposition of *Ascaris suum* in pigs.

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Tinghuan Song (Project B1, HUB)

Hello you all! My name is Tinghuan Song. In October 2020, I finished my master's degree in human biology at the University of Copenhagen. A few months later in April 2021, I moved to Berlin and officially joined GRK2046. Currently I work under the supervision of Prof. Dr. Kai Matuschewski and Dr. Katja Müller at Humboldt-Universität zu Berlin. My interests mainly focus on the immune correlates of protective immunity against *Plasmodium* infection, and next-generation malaria vaccine development. I will apply multiple computational, immunological, and genetic approaches *in silico*, *in vitro* and *in vivo* to discover novel CD8+ T cell epitopes from *Plasmodium berghei*, followed by the design of a viral vector-based vaccine containing the best candidate epitopes which could elicit strong protective immunity against *Plasmodium* infection.

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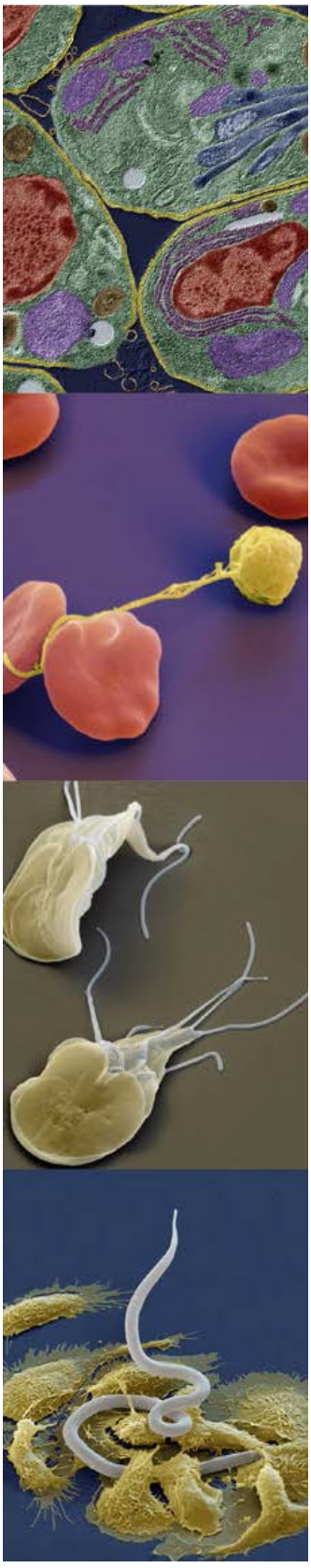


Conferences & Workshops

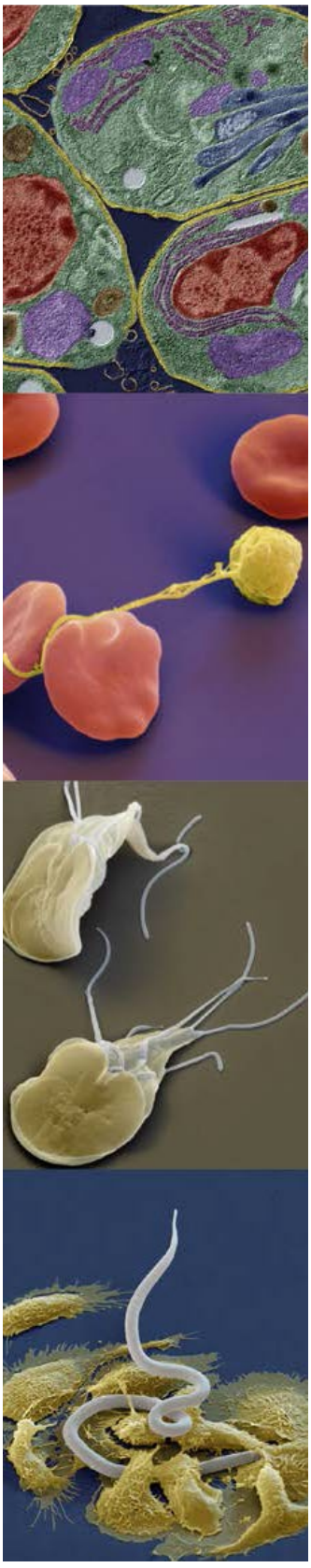
29th Annual Meeting of the German Society for Parasitology

March 15-17, 2021, ONLINE

The 29th Annual Meeting of the German Society for Parasitology, which was originally scheduled to be held in Bonn in 2020, was postponed to be held online this year. This made us look forward to the conference even more. And most of us have actively participated in the conference and introduced our recent work in the related session and received useful feedback.

During the conference, 15 invited keynote speakers talked about their recent work on six topics including anti-helmintic drug development, one health, helminth immunology and wildlife immunology. In addition, around 300 participants introduced their recent results in 24 oral presentation sessions and 18 poster sessions respectively. The GRK2046 organized a workshop on the theme of 'wildlife parasitology' as part of the conference. Miguel, Sophia and I participated in organizing the workshop, I was very honored and rewarded. Our workshop received an active participation of researchers in related fields. In order to allow all contributors to show their work, participants who were not selected in the main session were arranged in the poster session where they can also have an opportunity to present their posters briefly. In main session, two invited keynote speakers, Prof. Eleanor Riley (Edinburgh) and Prof. Joseph Jackson (Salford), and five other speakers introduced their recent wok, and received positive responses and feedback from the audience.

Taken from https://dgparasitologie.de/



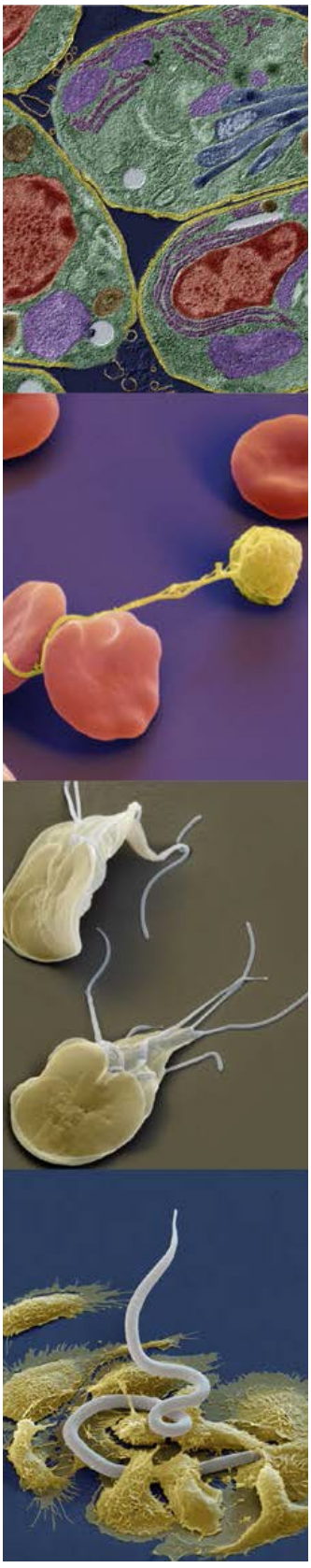
The conference was a complete success. In my opinion, online meetings have certain advantages, they save the burden and expenses of travel, especially for participants from countries far away from Europe. The interface of this meeting is also very friendly which exceeded my expectations. However, online meetings are also inadequate. Due to the lack of face-to-face communication, the connection between speakers and audience has become weak, and due to the compact agenda, few people can participate in the separate discussion meeting after the talks, which is disappointing. I still look forward to the next annual meeting, where we can meet face to face to better communicate and share our work.

– Hongwei Zhang

GRK 2046 Workshop @29th Annual Meeting of the German Society for Parasitology

March 15-17, 2021, ONLINE

Within the framework of 29th annual meeting of the German Society of Parasitology, the GRK2046 had once again the privilege of organising a workshop that would bring together well-acknowledged researchers and PhD candidates. The topic chosen for this edition was “Wildlife Parasitology”, which we recognised to be often underrepresented in similar meetings and which we expected to raise interest even among participants not directly working on wildlife, particularly in times of pandemic when the concept of One Health is, again, called for. The attendees witnessed two inspiring key-note talks, by Professor Eleanor Riley (Institute of Immunology and Infection Research, University of Edinburgh), who gave a comprehensive insight into comparative immunology in wild and laboratory mice, and by Professor Joseph Jackson (School of Science, Engineering and Environment, University of Salford), who addressed challenges in performing immunology studies in non-model organisms, and to which extent they can be overcome.



Screenshot by Miguel Veiga

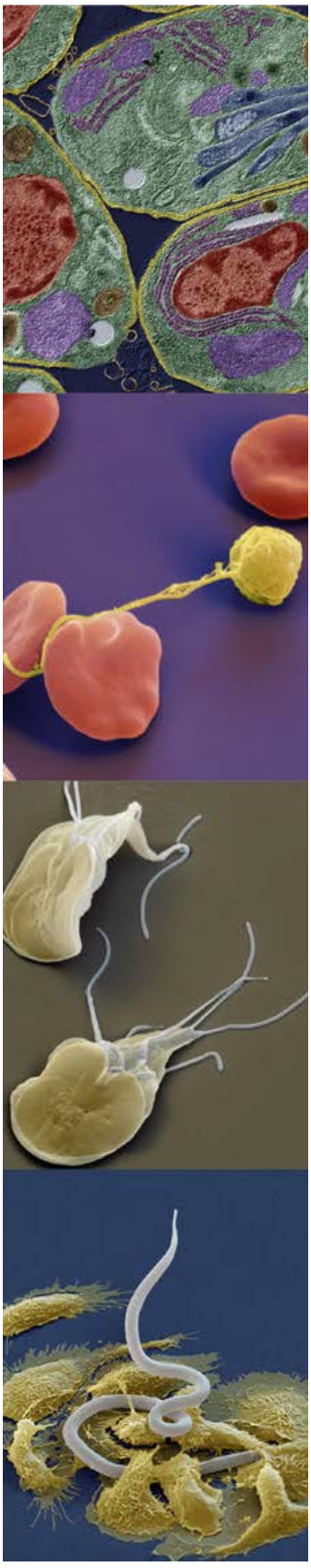
Parasite species addressed in other presentations were diverse and included trematodes, nematodes and protozoa. Each talk was followed by an actively participated Q&A session, and, after the closing of the workshop, a general discussion was open to all interested participants wanting to further extend the discussion. We are quite pleased with the quality of the presentations and with the attendance, which motivates us GRK2046 to start thinking of challenging topics for the upcoming 30th DGP annual meeting. We would like to express our gratitude to Susanne Hartmann, Sebastian Rausch and Marko Janke for endorsing our topic and for their support throughout the organisational process!

– Miguel Veiga

14th International Symposium on Ticks and Tick-borne Diseases

March 24-26, 2021, ONLINE

The objective of the Symposium is to jointly discuss research advances made in the subject area of ticks and tick-borne diseases. Normally, it takes place every two years, in Weimar, where people flew in from all over the world. This year, due to Corona, it had to be held online, and



even if it is always good visited from international scientist from all over the world, the online format gave the opportunity to more scientists from distant countries to assist. The fact that it was online, made it be at different hours than we are used in presence. It started at 12 am and finished at around 9 pm, in order to respect all time zones for the maximal possible assistants. The conference was distributed in different scientific sessions and poster sessions, facing topics as Tick-borne Encephalitis, Lyme Borreliosis, Tick biology, and tick-borne pathogen interaction, among others. The conference is also known for their prestigious Sinnecker-Kunt award, where early-career researchers have the opportunity to show their advances in research. Twelve candidates competed for the prize, with 1st, 2nd and 3rd position. The only missed thing was socializing and exchanging with other participants, due to the online format and probably the main reason why we are all looking forward to events in present again.

– Sophia Pinecki

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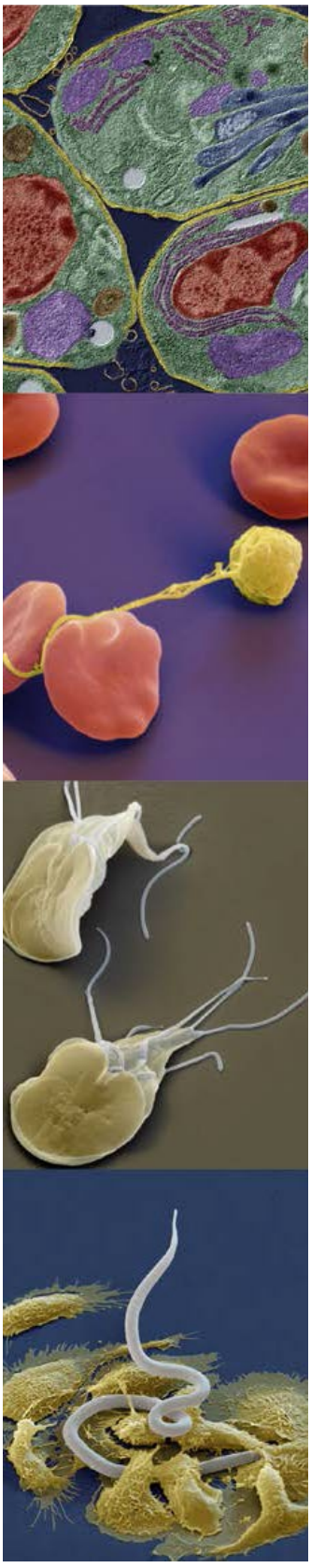
15. Kongress für Infektionskrankheiten und Tropenmedizin mit 28. Jahrestagung der DGPI

June 16-19, 2021, ONLINE

It was a pleasure to attend the 15th congress of Infectious Diseases and Tropical Medicine (Kongress fuer Infektionskrankheiten und Tropenmedizin; KIT) at the beginning of June 2021. While enduring tropical temperatures in Berlin, I undertook a virtual discovery journey through the German network of infectiology. The congress covered a wide variety of topics, and the digital set-up allowed me to hop from Antibiotic Stewardship, to the vaccine debate, to Digital Health, to Ebola… And off course our Charité Institute of Tropical Medicine and International Health was well represented!



KIT2021

PROGRAMM **DONNERSTAG, 17. JUNI 2021**

13.15 – 14.15 **Symposium**
SY22 **Free Paper IV – DTG**
Virtual Hall V *Vorsitz: N. Gilberger, Hamburg*
A. Abd El Wahed, Leipzig

13.15 FV21 **Predictive performance of rapid diagnostic tests for falciparum malaria and its modelled impact on integrated community case management of malaria in sub-Saharan African febrile children**
J. Mischlinger, V. Dudek, M. Ramharter
Hamburg

13.20 FV22 **The first record of the invasive mosquito Aedes albopictus in the Republic of Moldova**
T. Sulesco
Chisinau

13.25 FV23 **Quantification of the proportion of unfavorable clinical outcomes among imported malaria patients according to the degree of semi-immunity on population level – an ecological study**
T. Nordmann, S. Davi, M. Ramharter, J. Mischlinger
Hamburg

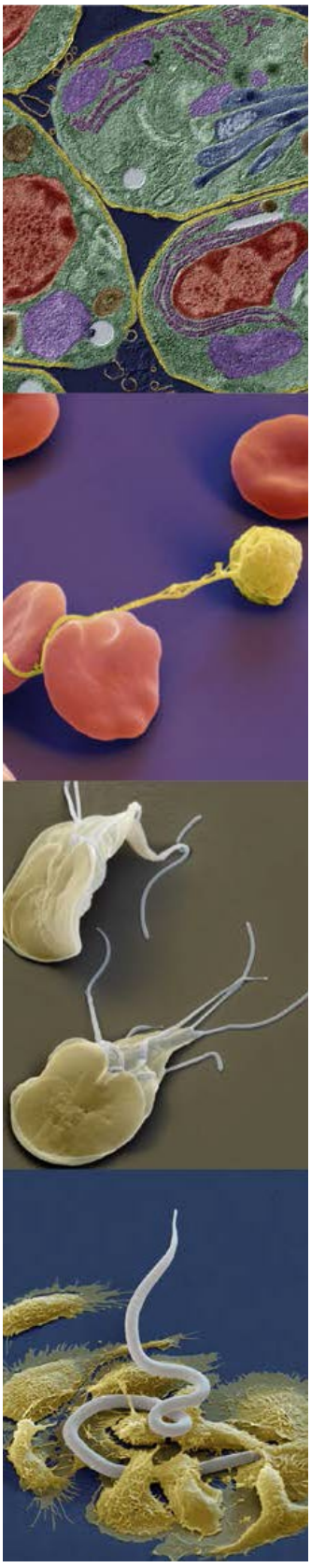
13.30 FV24 **Changing patterns in Plasmodium falciparum multidrug resistance-1 gene polymorphisms over the last decade in southern Rwanda**
W. van Loon[1], C. Bergmann[1], F. Habarugira[2], C. Tacoli[1], D. Savelsberg[1], R. Santos de Oliveira[1], D. Mbarushimana[2], J. Ndoli[2], A. Sendegeya[2], C. Bayingana[2], F. Mockenhaupt[1]
[1]Berlin, [2]Huye

DONNERSTAG, 17. JUNI 2021 DONNERSTAG

Extract from official KIT 2021 program

The talks given by my colleagues and me demonstrates the extensive range of topics we touch in the field of global health (including Berliner Corona School Study (BECOSS), Berliner Corona Self-Swab Study, COVID-19 project for the homeless in Berlin, COVID-19 in Uganda, sonography in schistosomiasis, care of patients with cystic echinococcosis, PVL-positive MRSA patients' perspectives, Antimicrobial Stewardship, host genetics and malaria in Ghana and India, and patterns in molecular markers of resistance in *P. falciparum* in Rwanda (me)). Even though virtual, the KIT realized a lively congress in which ideas, perspectives and results were exchanged and discussed between various disciplines. And this is exactly what we need to move to a One Health approach to achieve better public health outcomes globally.

– Welmoed van Loon



Berlin University Alliance (BUA) Retreat

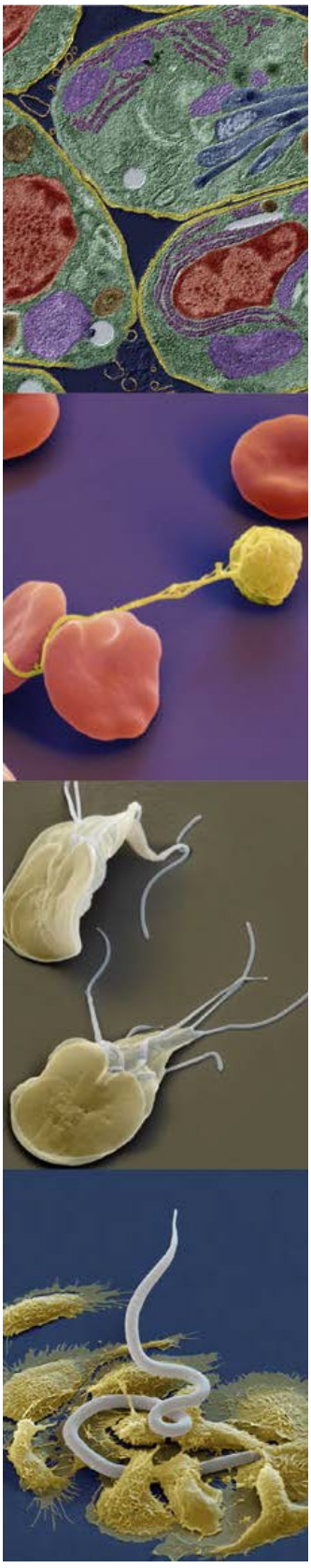
May 3-6, 2021, ONLINE

The Berlin university alliance (BUA) offered a retreat this year inviting students from different disciplines from the major universities of Berlin. The event was specifically designed for early career researchers in the beginning of their PhD and focused on a wide range of topics. After introduction of the academic career path and german labour market, any international speakers presented their expertise on topics like time management, self motivation, relaxation, and worklife balance. Furthermore, the event informed us about the process of scientific writing - with the different styles of scientific texts, methods to find the wright dissertation topic, and techniques to stay in a creative mindset. Especial emphasis was put on social networking as basis of scientific discussion and exchange amongst colleagues. After an introductory session, students were put in breakout rooms to become acquainted amongst themselves, allowing a practical approach or simple chats with others from a broad spectrum of scientific fields. Network events in the evening created another chance to meet in a more casual setting and one on one coaching sessions with the speakers permitted personalised training. Even though the shortness of the talks did not allow to go into much depth, the retreat addressed many important topics for PhD students outside of their scientific topics. It created a conversation between students from the humanities, social and natural sciences and gave the opportunity to get to know new people also starting their PhD in Berlin.

– Otto Netzel

Official Logo BUA, taken from https://www.drs.fu-berlin.de/node/50850/

From May 3-6 I attended a retreat called “kick off your doctorate” organized by Berlin University Alliance. It was aimed for early-stage doctoral researchers. Due to the pandemic, it was online this year. It covered a wide range of topics, including culture, networking, career planning, writings, self-management and so on. Besides, we also got



private opportunities to ask about anything we would like to know. On the bright side, it was a good chance to meet fellow PhD students across all the institutes in Berlin and exchange ideas with them, but due to its online form, it was not as interactive as in person. I would recommend it to those fellow students who are at their early-stage of research and eager to expand their networks and make new friends.

– Tinghuan Song

Berlin Parasitology Seminars (BPS)

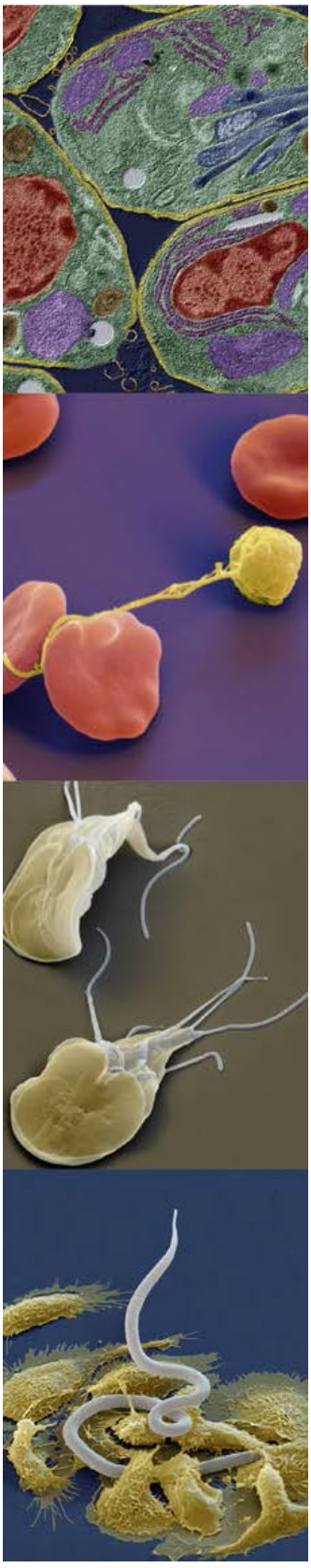
Stephen Doyle
Wellcome Sanger Institute, Cambridge, United Kingdom

13th April 2021 (online)

Dr. Stephen Doyle from the Wellcome Sanger Institute in Cambridge gave a fascinating talk entitled “Using genomics to map drug resistance genes in a globally important gastrointestinal parasite”. Stephen and his lab are working on genomic approaches to understand the genetic basis for the evolutionary success of parasitic worms, such as the development of drug resistance mechanisms.

In his talk, Stephen gave us insights into his latest work on elucidating the drug resistance mechanisms of the blood-sucking nematode *Haemonchus contortus*. By performing back-crossing experiments of highly resistant isolate into a susceptible background over multiple generations and treating with different anthelmintics, they could select progeny with resistance-associated genes. The following genomic sequencing of the progeny identified specifically selected regions in the genome which led to the assumption that no single gene but multiple can be associated with resistance, particularly for macrocyclic lactones. Primarily the treatment with ivermectin led to the upregulation of kinases and transcription factors. The resulting candidate genes will be further tested to confirm the genomic and transcriptomic data. In the case of benzimidazole treatment, the already known beta-Tubulin gene was selected and confirmed no additional resistance mechanism for this drug class.

– Natalie Jakobs



Rosalind Laing
University of Glasgow, Scotland

11th May 2021 (online)

Dr. Rosalind Laing from the Institute of Biodiversity, Animal Health & Comparative Medicine of the University of Glasgow gave a talk entitled "Genomic and transcriptomic analysis of resistance to anthelmintic drugs in a parasitic nematode". Her research mainly focuses on the molecular biology and genetic basis of parasite drug resistance.

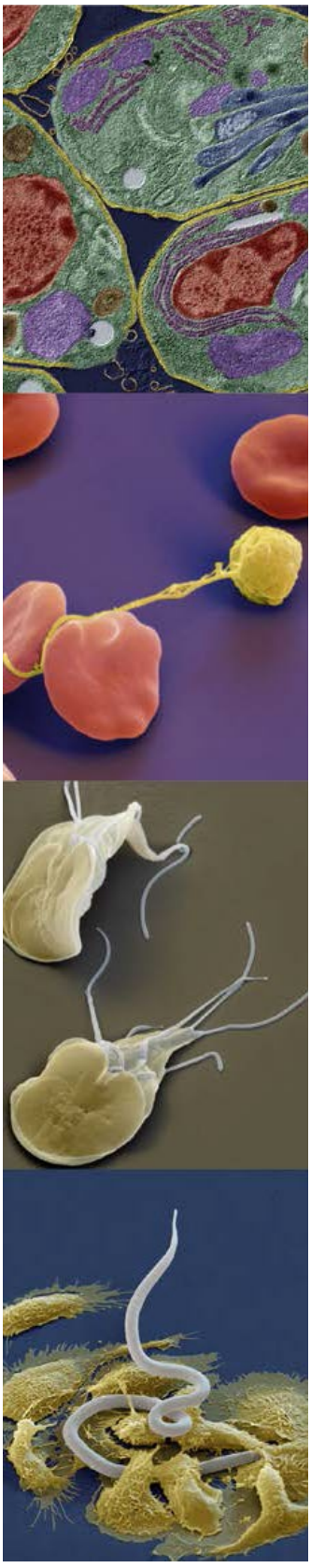
Dr. Rosalind Laing is closely working together with Dr. Stephen Doyle. Therefore, her talk mainly focused on elucidating the genetic basis of *Haemonchus contortus* drug resistance on a molecular biology level. After a genome-wide differential gene expression analysis of genetically crossed highly resistant and susceptible *H. contortus* isolates, a transcription factor was identified as mostly highly upregulated. Using a *Caenorhabditis elegans* knock-out strain and performing RNAi, Laing and her group confirmed this gene to influence the susceptibility towards the macrocyclic lactone. However, transgenic expression of this *H. contortus* gene in *C. elegans* did not lead to significant results, wondering if *C. elegans* is an appropriate model to study parasitic drug resistance mechanisms. In the future, her group wants to establish RNAi in parasitic nematodes.

– Natalie Jakobs

Kara Filbey
The University of Manchester, United Kingdom

8th June 2021 (online)

For the June edition of our BPS series we were joined by Dr. Kara Filbey as a virtual guest. Dr. Filbey is currently a Research Associate at the Division of Infection, Immunity & Respiratory Medicine at the University of Manchester in the UK. She has a long-standing research interest in helminth infection-related innate immunity, immune regulation and allergic inflammation. In her talk titled "The varied faces of helminth immunomodulation" Dr. Filbey gave a comprehensive and very exciting overview of her past work on *H. polygyrus*-drived suppression of skin



inflammation and on nematode-induced lung immunity against distinct helminths in coinfection settings using *H. polygyrus* and *N. brasiliensis* in mice. During the afternoon before her talk several GRK2046 members also had the opportunity to meet with our BPS guest virtually for more informal discussions of individual GRK2046 projects, marking another successful and insightful (virtual) BPS seminar!

– Ivet Yordanova

Upcoming Talks

Berlin Parasitology Seminars

August 24, 2021, 5pm – Tim Geary (ONLINE)*

October 12, 2021, 5pm – Pedro H Gazzinelli-Guimaraes (ONLINE)*

October 26, 2021, 5pm – Guillaume Salle (ONLINE)*

November 09, 2021, 5pm – Elia Tait Wojno (ONLINE)*

December 07, 2021, 5pm – Aimee Taylor (ONLINE)*

December 14, 2021, 5pm – Jakob von Moltke (ONLINE)*

*ONLINE, maybe organized as in person event, if possible

Role Models in Infection Biology

September 21, 2021, 9am# – Flaminia Catteruccia (Mitte or ONLINE)*

October 19, 2021, 9am – Kerstin Mair (Düppel or ONLINE)*

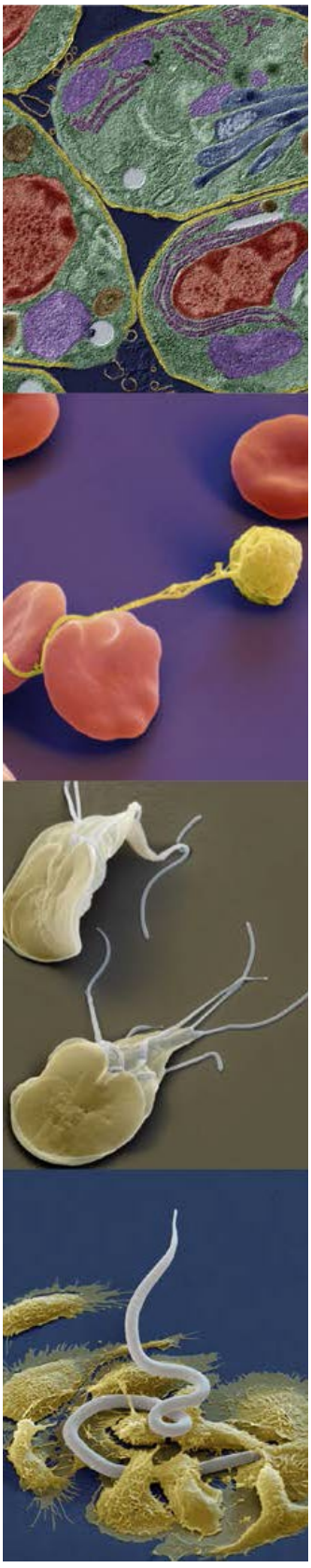
October 25, 2021, 9am – Dame Sally Davies (Mitte or ONLINE)*

November 23, 2021, 9am – Sophie Duraffour (Mitte or ONLINE)*

February 15, 2022, 9am – Sophie Armitage (Düppel or ONLINE)*

* in person event, maybe organized ONLINE

#9am CET when in person, likely 5pm CET when ONLINE



Graduated 1st generation students and date of defense

Victor Hugo Jarquín Díaz – 02.02.2021

Congratulations!

Assessment centers, December 2020 - June 2021

Finally, we filled the three remaining vacant positions in our GRK. In additional assessment centers end of 2020 / beginnig of 2021 we found excellent candidates. Unfortunetaly, due to the travel restrictions in the pandemic several new PhD students from overseas had severe trouble in gaining a visa to enter Germany and therefore started here delayed.

– Marko

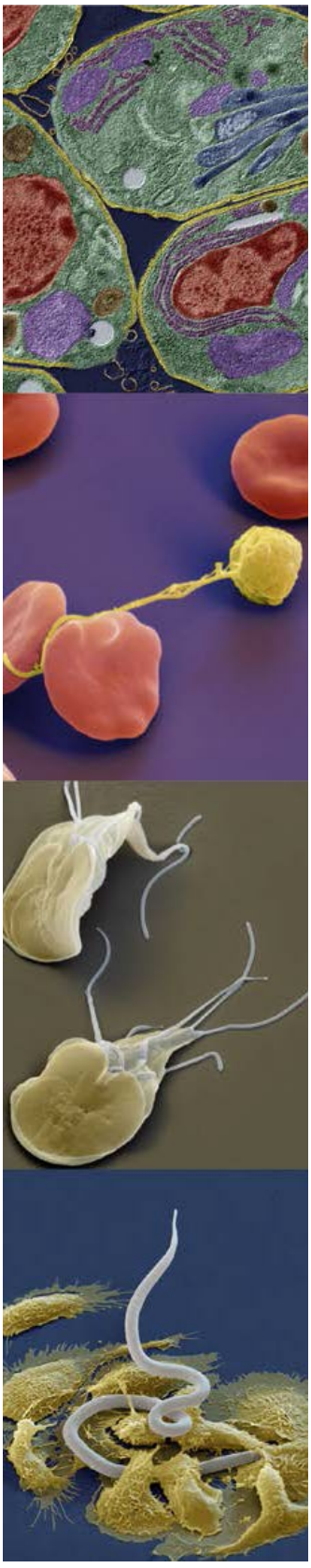
Publications

Increase in Kelch 13 Polymorphisms in *Plasmodium falciparum*, Southern Rwanda

Bergmann C, **van Loon W**, Habarugira F, **Tacoli C**, Jäger JC, Savelsberg D, Nshimiyimana F, Rwamugema E, Mbarushimana D, Ndoli J, Sendegeya A, Bayingana C, **Mockenhaupt FP**. (2021).

Emerg Infect Dis *27:294–6. doi: 10.3201/eid2701.203527.*

Abstract:
Artemisinin resistance in *Plasmodium falciparum* is associated with nonsynonymous mutations in the Kelch 13 (K13) propeller domain. We found that 12.1% (8/66) of clinical *P. falciparum* isolates from Huye district, Rwanda, exhibited K13 mutations, including R561H, a validated resistance marker. K13 mutations appear to be increasing in this region.



Pharyngeal Pumping and Tissue-Specific Transgenic P-Glycoprotein Expression Influence Macrocyclic Lactone Susceptibility in *Caenorhabditis elegans*

Gerhard AP, **Krücken J**, Neveu C. Charvet CL, Harmache A, **von Samson-Himmelstjerna G**. (2021).

Pharmaceuticals 14:153. doi: 10.3390/ph14020153.

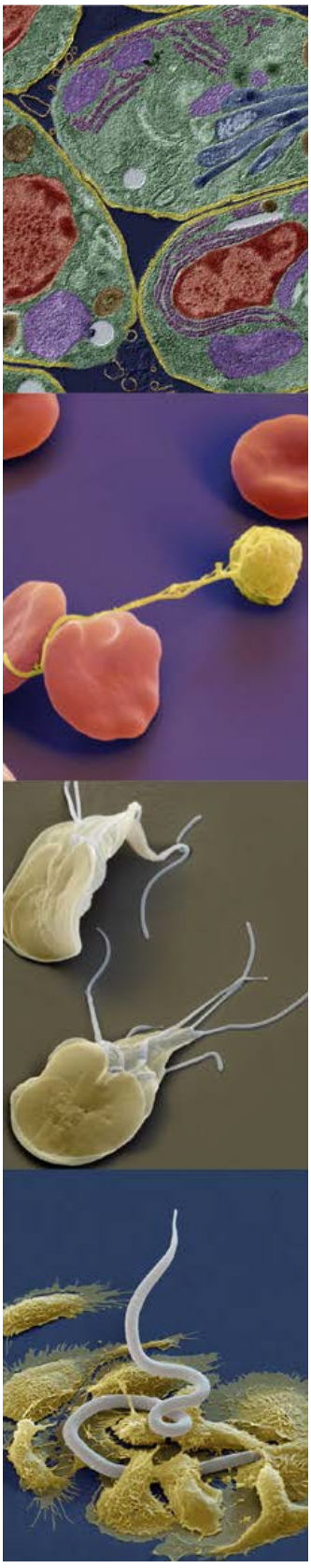
Abstract:
Macrocyclic lactones (MLs) are widely used drugs to treat and prevent parasitic nematode infections. In many nematode species including a major pathogen of foals, *Parascaris univalens*, resistance against MLs is widespread, but the underlying resistance mechanisms and ML penetration routes into nematodes remain unknown. Here, we examined how the P-glycoprotein efflux pumps, candidate genes for ML resistance, can modulate drug susceptibility and investigated the role of active drug ingestion for ML susceptibility in the model nematode *Caenorhabditis elegans*. Wildtype or transgenic worms, modified to overexpress *P. univalens* PGP-9 (Pun-PGP-9) at the intestine or epidermis, were incubated with ivermectin or moxidectin in the presence (bacteria or serotonin) or absence (no specific stimulus) of pharyngeal pumping (PP). Active drug ingestion by PP was identified as an important factor for ivermectin susceptibility, while moxidectin susceptibility was only moderately affected. Intestinal Pun-PGP-9 expression elicited a protective effect against ivermectin and moxidectin only in the presence of PP stimulation. Conversely, epidermal Pun-PGP-9 expression protected against moxidectin regardless of PP and against ivermectin only in the absence of active drug ingestion. Our results demonstrate the role of active drug ingestion by nematodes for susceptibility and provide functional evidence for the contribution of P-glycoproteins to ML resistance in a tissue-specific manner.

Expanding the Known Repertoire of C-Type Lectin Receptors Binding to Toxoplasma gondii Oocysts Using a Modified High-Resolution Immunofluorescence Assay

Fabian BT, Lepenies B, Schares G, Dubey JP, Spano F, **Seeber F**. (2021).

mSphere 6:e01341-20. doi: 10.3390/ph14020153.

Abstract:
The environmental stage of the apicomplexan *Toxoplasma gondii* oocyst is vital to its life cycle but largely understudied. Because oocysts are excreted only by infected felids, their availability for research is limited. We report the adaptation of an agarose-based method to immobilize minute amounts of oocysts to perform immunofluorescence assays. Agarose embedding allows high-resolution confocal microscopy imaging of antibodies binding to the oocyst



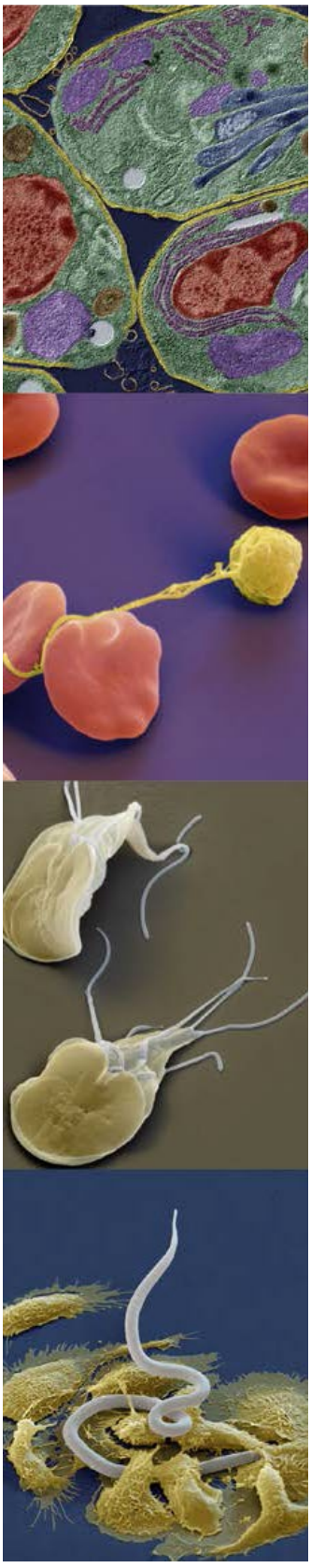
surface as well as unprecedented imaging of intracellular sporocyst structures with *Maclura pomifera* agglutinin after on-slide permeabilization of the immobilized oocysts. To identify new possible molecules binding to the oocyst surface, we used this method to screen a library of C-type lectin receptor (CLR)-human IgG constant region fusion proteins from the group of related CLRs called the Dectin-1 cluster against oocysts. In addition to CLEC7A that was previously reported to decorate *T. gondii* oocysts, we present experimental evidence for specific binding of three additional CLRs to the surface of this stage. We discuss how these CLRs, known to be expressed on neutrophils, dendritic cells, or macrophages, could be involved in the early immune response by the host, such as oocyst antigen uptake in the intestine. In conclusion, we present a modified immunofluorescence assay technique that allows material-saving immunofluorescence microscopy with *T. gondii* oocysts in a higher resolution than previously published, which allowed us to describe three additional CLRs binding specifically to the oocyst surface.IMPORTANCE Knowledge of oocyst biology of *Toxoplasma gondii* is limited, not the least due to its limited availability. We describe a method that permits us to process minute amounts of oocysts for immunofluorescence microscopy without compromising their structural properties. This method allowed us to visualize internal structures of sporocysts by confocal microscopy in unprecedented quality. Moreover, the method can be used as a low- to medium-throughput method to screen for molecules interacting with oocysts, such as antibodies, or compounds causing structural damage to oocysts (i.e., disinfectants). Using this method, we screened a small library of C-type lectin receptors (CLRs) present on certain immune cells and found three CLRs able to decorate the oocyst wall of *T. gondii* and which were not known before to bind to oocysts. These tools will allow further study into oocyst wall composition and could also provoke experiments regarding immunological recognition of oocysts.

Genetic variability, cryptic species and phylogenetic relationship of six cyathostomin species based on mitochondrial and nuclear sequences

Louro M, Kuzmina TA, **Bredtmann CM**, **Diekmann I**, de Carvalho LMM, **von Samson-Himmelstjerna G**, **Krücken J**. (2021).

Sci Rep 11:8245. doi: 10.1038/s41598-021-87500-8.

Abstract:
Cyathostomins are important intestinal nematode parasites of equines and include 50 accepted species. Their taxonomy has been frequently revised and the presence of cryptic species suggested. Furthermore, usually molecular- and morphology-based phylogenetic analyses give divergent results. In this study, the nucleotide sequences of the nuclear second internal transcribed spacer (ITS-2) and the mitochondrial partial cytochrome c oxidase subunit I (COI) were determined for adults of six cyathostomin species (*Coronocyclus coronatus*, *Coronocyclus labiatus*, *Cylicocyclus nassatus*, *Cylicostephanus calicatus*, *Cylicostephanus longibursatus*, *Cylicostephanus minutus*) collected from



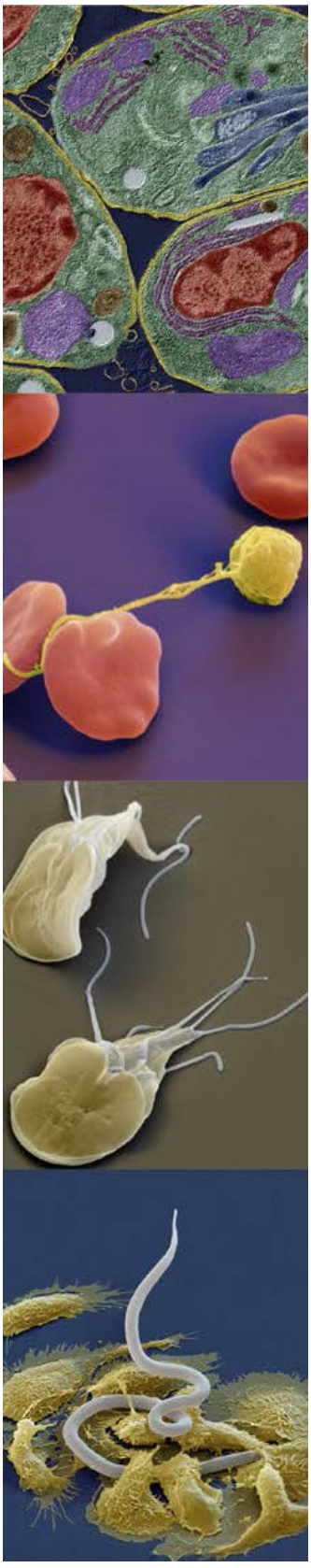
different equine species within two geographic regions. Maximum likelihood trees were calculated for ITS-2, COI, and concatenated data. No obvious differentiation was observed between geographic regions or equine host species. As previously reported, *Coronocyclus coronatus* and *Cylicostephanus calicatus* revealed a close relationship. Cryptic species were detected in *Cylicostephanus minutus* and *Cylicostephanus calicatus*. *Cylicocyclus nassatus* and *Coronocyclus labiatus* showed diverse mitochondrial and nuclear haplotypes occurring in different combinations, while *Cylicostephanus longibursatus* was comparatively homogenous. In conclusion, a combined analysis of nuclear and mitochondrial haplotypes improved resolution of the phylogeny and should be applied to the remaining cyathostomin species and across additional equine host species and geographic regions.

Molecular analysis suggests that Namibian cheetahs (*Acinonyx jubatus*) are definitive hosts of a so far undescribed *Besnoitia* species

Schares G, Joeres M, Rachel F, Tuschy M, **Czirják GÁ**, Maksimov P, Conraths FJ, **Wachter B**. (2021).

Parasit Vectors 14:201. doi: 10.1186/s13071-021-04697-3.

Abstract:
Background: *Besnoitia darlingi*, *B. neotomofelis* and *B. oryctofelisi* are closely related coccidian parasites with felids as definitive hosts. These parasites use a variety of animal species as intermediate hosts. North American opossums (*Didelphis virginiana*), North American southern plains woodrats (*Neotoma micropus*) and South American domestic rabbits (*Oryctolagus cuniculus*) are intermediate hosts of *B. darlingi*, *B. neotomofelis* and *B. oryctofelisi*, respectively. Based on conserved regions in the internal transcribed spacer-1 (ITS1) sequence of the ribosomal DNA (rDNA), a real-time PCR for a sensitive detection of these *Besnoitia* spp. in tissues of intermediate hosts and faeces of definitive hosts has recently been established. Available sequence data suggest that species such as *B. akodoni* and *B. jellisoni* are also covered by this real-time PCR. It has been hypothesised that additional *Besnoitia* spp. exist worldwide that are closely related to *B. darlingi* or *B. darlingi*-like parasites (*B. neotomofelis*, *B. oryctofelisi*, *B. akodoni* or *B. jellisoni*). Also related, but not as closely, is *B. besnoiti*, the cause of bovine besnoitiosis. **Methods**: Faecal samples from two free-ranging cheetahs (*Acinonyx jubatus*) from Namibia that had previously tested positive for coccidian parasites by coproscopy were used for this study. A conventional PCR verified the presence of coccidian parasite DNA. To clarify the identity of these coccidia, the faecal DNA samples were further characterised by species-specific PCRs and Sanger sequencing. **Results**: One of the samples tested positive for *B. darlingi* or *B. darlingi*-like parasites by real-time PCR, while no other coccidian parasites, including *Toxoplasma gondii*, *Hammondia hammondi*, *H. heydorni*, *B. besnoiti* and *Neospora caninum*, were detected in the two samples. The rDNA of the *B. darlingi*-like parasite was amplified and partially sequenced. Comparison with



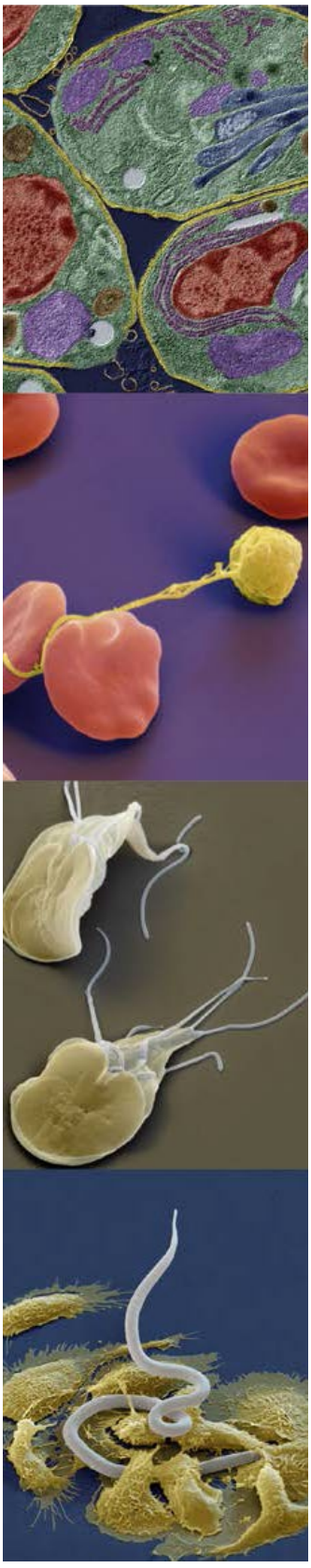
existing sequences in GenBank revealed a close relationship to other *Besnoitia* spp., but also showed clear divergences. **Conclusions**: Our results suggest that a so far unknown *Besnoitia* species exists in Namibian wildlife, which is closely related to *B. darlingi*, *B. neotomofelis*, *B. oryctofelisi*, *B. akodoni* or *B. jellisoni*. The cheetah appears to be the definitive host of this newly discovered parasite, while prey species of the cheetah may act as intermediate hosts.

Harmonization of Protocols for Multi-Species Organoid Platforms to Study the Intestinal Biology of *Toxoplasma gondii* and Other Protozoan Infections

Holthaus D, **Delgado-Betancourt E**, **Aebischer T**, **Seeber F**, **Klotz C**. (2021).

Front Cell Infect Microbiol 10:610368. doi: 10.3389/fcimb.2020.610368.

Abstract:
The small intestinal epithelium is the primary route of infection for many protozoan parasites. Understanding the mechanisms of infection, however, has been hindered due to the lack of appropriate models that recapitulate the complexity of the intestinal epithelium. Here, we describe an *in vitro* platform using stem cell-derived intestinal organoids established for four species that are important hosts of Apicomplexa and other protozoa in a zoonotic context: human, mouse, pig and chicken. The focus was set to create organoid-derived monolayers (ODMs) using the transwell system amenable for infection studies, and we provide straightforward guidelines for their generation and differentiation from organ-derived intestinal crypts. To this end, we reduced medium variations to an absolute minimum, allowing generation and differentiation of three-dimensional organoids for all four species and the subsequent generation of ODMs. Quantitative RT-PCR, immunolabeling with antibodies against marker proteins as well as transepithelial-electrical resistance (TEER) measurements were used to characterize ODM's integrity and functional state. These experiments show an overall uniform generation of monolayers suitable for *Toxoplasma gondii* infection, although robustness in terms of generation of stable TEER levels and cell differentiation status varies from species to species. Murine duodenal ODMs were then infected with *T. gondii* and/or *Giardia duodenalis*, two parasites that temporarily co-inhabit the intestinal niche but have not been studied previously in cellular co-infection models. *T. gondii* alone did not alter TEER values, integrity and transcriptional abundance of tight junction components. In contrast, in *G. duodenalis*-infected ODMs all these parameters were altered and *T. gondii* had no apparent influence on the *G. duodenalis*-triggered phenotype. In conclusion, we provide robust protocols for the generation, differentiation and characterization of intestinal organoids and ODMs from four species. We show their applications for comparative studies on parasite-host interactions during the early phase of a *T. gondii* infection but also its use for co-infections with other relevant intestinal protozoans.



Artificial Feeding of All Consecutive Life Stages of *Ixodes ricinus*

Militzer N, Bartel A , Clausen PH, Hoffmann-Köhler P, Nijhof AM. (2021).

Vaccines *9:385. doi: 10.3390/vaccines904038*.

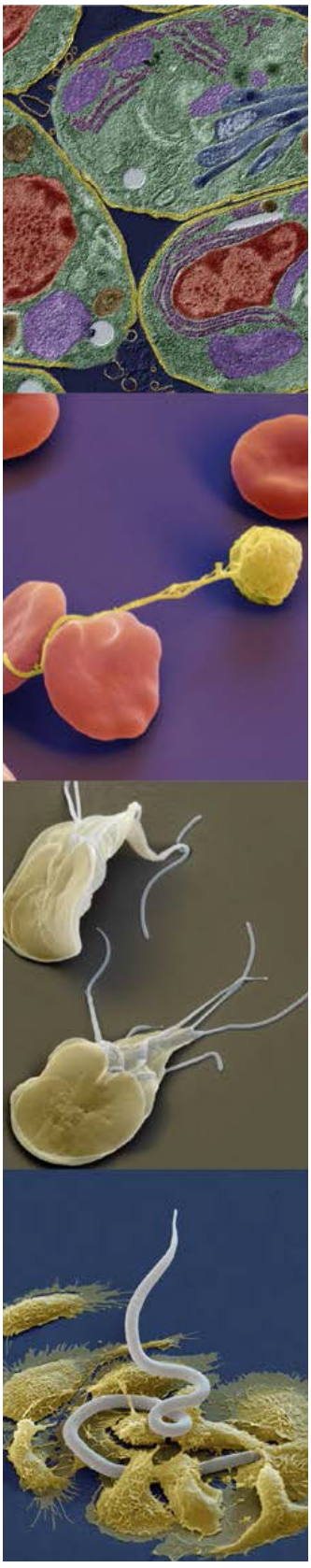
Abstract:
The hard tick *Ixodes ricinus* is an obligate hematophagous arthropod and the main vector for several zoonotic diseases. The life cycle of this three-host tick species was completed for the first time *in vitro* by feeding all consecutive life stages using an artificial tick feeding system (ATFS) on heparinized bovine blood supplemented with glucose, adenosine triphosphate, and gentamicin. Relevant physiological parameters were compared to ticks fed on cattle (*in vivo*). All *in vitro* feedings lasted significantly longer and the mean engorgement weight of F0 adults and F1 larvae and nymphs was significantly lower compared to ticks fed *in vivo*. The proportions of engorged ticks were significantly lower for *in vitro* fed adults and nymphs as well, but higher for *in vitro* fed larvae. F1-females fed on blood supplemented with vitamin B had a higher detachment proportion and engorgement weight compared to F1-females fed on blood without vitamin B, suggesting that vitamin B supplementation is essential in the artificial feeding of *I. ricinus* ticks previously exposed to gentamicin.

Noninvasively measured immune responses reflect current parasite infections in a wild carnivore and are linked to longevity

Ferreira SCM, **Veiga MM**, **Hofer H**, **East ML**, **Czirják GÁ**. (2021).

Ecol Evol 00:1-15. doi: 10.1002/ece3.7602.

Abstract:
Host immune defenses are important components of host–parasite interactions that affect the outcome of infection and may have fitness consequences for hosts when increased allocation of resources to immune responses undermines other essential life processes. Research on host–parasite interactions in large free-ranging wild mammals is currently hampered by a lack of verified noninvasive assays. We successfully adapted existing assays to measure innate and adaptive immune responses produced by the gastrointestinal mucosa in spotted hyena (*Crocuta crocuta*) feces, including enzyme-linked immunosorbent assays (ELISAs),to quantify fecal immunoglobulins (total IgA, total IgG) and total fecal O-linked oligosaccharides (mucin). We investigated the effect of infection load by an energetically costly hookworm (*Ancylostoma*), parasite richness, host age, sex, year of sampling, and clan membership on immune responses and asked whether high investment in immune responses during early life affects longevity in individually known spotted hyenas in the Serengeti National Park, Tanzania. Fecal concentrations of IgA, IgG, and mucin increased with *Ancylostoma* egg load and were higher in juveniles than in



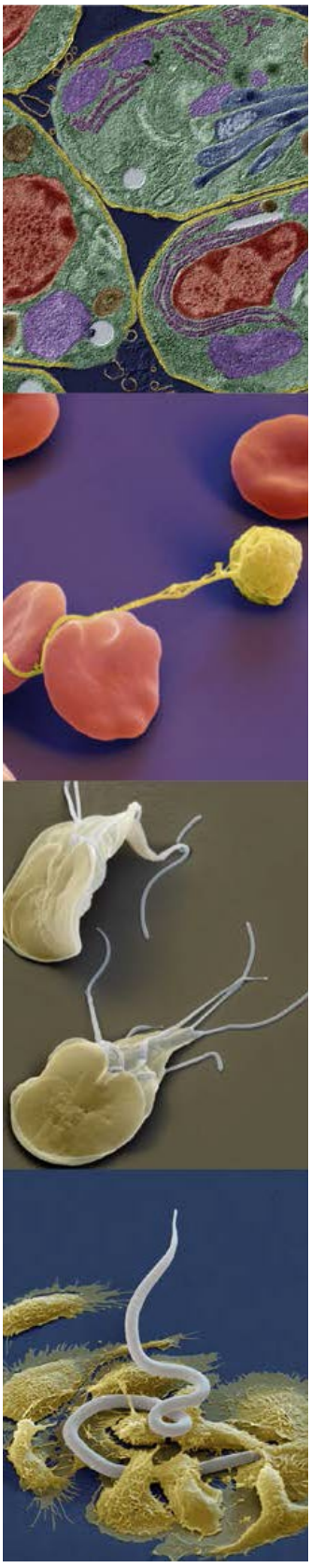
adults. Females had higher mucin concentrations than males. Juvenile females had higher IgG concentrations than juvenile males, whereas adult females had lower IgG concentrations than adult males. High IgA concentrations during the first year of life were linked to reduced longevity after controlling for age at sampling and *Ancylostoma* egg load. Our study demonstrates that the use of noninvasive methods can increase knowledge on the complex relationship between gastrointestinal parasites and host local immune responses in wild large mammals and reveal fitness-relevant effects of these responses.

Genetic diversity of vector-borne pathogens in spotted and brown hyenas from Namibia and Tanzania relates to ecological conditions rather than host taxonomy

Krücken J, **Czirják GÁ**, Ramünke S, **Serocki M**, Heinricht SK, Melzheimer J, Costa MC, **Hofer H**, Aschenborn OHK, Barker NA, Capodanno S, Madeira de Carvalho L, **von Samson-Himmelstjerna G**, **East ML**, **Wachter B**. (2021).

Parasit Vectors 14:328. doi: 10.1186/s13071-021-04835-x.

Abstract:
Background: Improved knowledge on vector-borne pathogens in wildlife will help determine their effect on host species at the population and individual level and whether these are affected by anthropogenic factors such as global climate change and landscape changes. Here, samples from brown hyenas (*Parahyaena brunnea*) from Namibia (BHNA) and spotted hyenas (*Crocuta crocuta*) from Namibia (SHNA) and Tanzania (SHTZ) were screened for vector-borne pathogens to assess the frequency and genetic diversity of pathogens and the effect of ecological conditions and host taxonomy on this diversity. **Methods:** Tissue samples from BHNA (n = 17), SHNA (n = 19) and SHTZ (n = 25) were analysed by PCRs targeting Anaplasmataceae, *Rickettsia* spp., piroplasms, specifically *Babesia lengau*-like piroplasms, Hepatozoidae and filarioids. After sequencing, maximum-likelihood phylogenetic analyses were conducted. **Results:** The relative frequency of Anaplasmataceae was significantly higher in BHNA (82.4%) and SHNA (100.0%) than in SHTZ (32.0%). Only *Anaplasma phagocytophilum*/*platys*-like and *Anaplasma bovis*-like sequences were detected. *Rickettsia raoultii* was found in one BHNA and three SHTZ. This is the first report of *R. raoultii* from sub-Saharan Africa. *Babesia lengau*-like piroplasms were found in 70.6% of BHNA, 88.9% of SHNA and 32.0% of SHTZ, showing higher sequence diversity than *B. lengau* from South African cheetahs (*Acinonyx jubatus*). In one SHTZ, a *Babesia vogeli*-like sequence was identified. Hepatozoon felis-like parasites were identified in 64.7% of BHNA, 36.8% of SHNA and 44.0% of SHTZ. Phylogenetic analysis placed the sequences outside the major *H. felis* cluster originating from wild and domestic felids. Filarioids were detected in 47.1% of BHNA, 47.4% of SHNA and 36.0% of SHTZ. Phylogenetic analysis revealed high genetic diversity and suggested the presence of several undescribed species. Co-infections were frequently detected in SHNA and BHNA (BHNA median 3 pathogens, range 1-



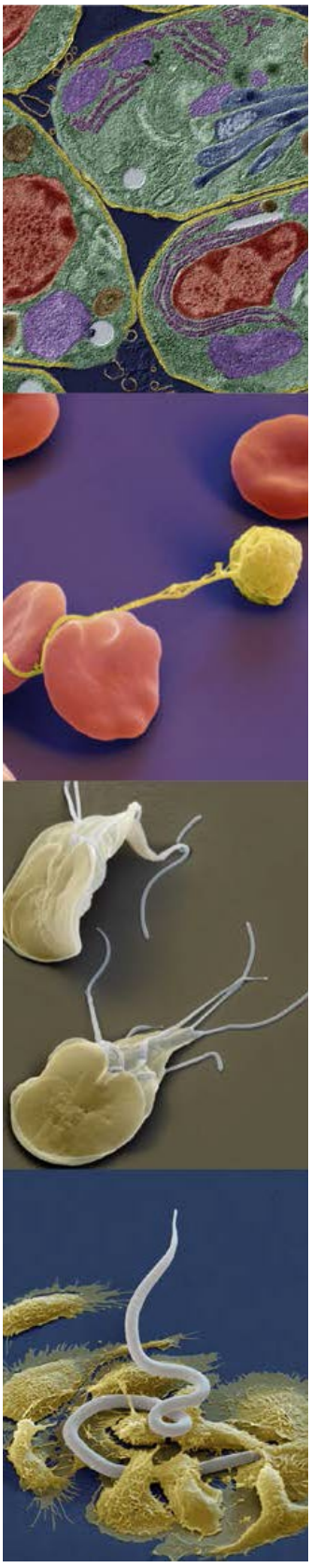
4; SHNA median 3 pathogens, range 2-4) and significantly rarer in SHTZ (median 1, range 0-4, 9 individuals uninfected). **Conclusions:** The frequencies of all pathogens groups were high, and except for *Rickettsia*, multiple species and genotypes were identified for each pathogen group. Ecological conditions explained pathogen identity and diversity better than host taxonomy.

The Worm-Specific Immune Response in Multiple Sclerosis Patients Receiving Controlled Trichuris suis Ova Immunotherapy

Yordanova IA, **Ebner F**, Schulz AR, **Steinfelder S**, Rosche B, Bolze A, Paul F, Mei HE, **Hartmann S**. (2021).

Life (Basel) 11:101. doi: 10.3390/life11020101.

Abstract:
Background: Improved knowledge on vector-borne pathogens in wildlife will help determine their effect on host species at the population and individual level and whether these are affected by anthropogenic factors such as global climate change and landscape changes. Here, samples from brown hyenas (*Parahyaena brunnea*) from Namibia (BHNA) and spotted hyenas (*Crocuta crocuta*) from Namibia (SHNA) and Tanzania (SHTZ) were screened for vector-borne pathogens to assess the frequency and genetic diversity of pathogens and the effect of ecological conditions and host taxonomy on this diversity. **Methods:** Tissue samples from BHNA (n = 17), SHNA (n = 19) and SHTZ (n = 25) were analysed by PCRs targeting Anaplasmataceae, *Rickettsia* spp., piroplasms, specifically *Babesia lengau*-like piroplasms, Hepatozoidae and filarioids. After sequencing, maximum-likelihood phylogenetic analyses were conducted. **Results:** The relative frequency of Anaplasmataceae was significantly higher in BHNA (82.4%) and SHNA (100.0%) than in SHTZ (32.0%). Only *Anaplasma phagocytophilum*/*platys*-like and *Anaplasma bovis*-like sequences were detected. *Rickettsia raoultii* was found in one BHNA and three SHTZ. This is the first report of *R. raoultii* from sub-Saharan Africa. *Babesia lengau*-like piroplasms were found in 70.6% of BHNA, 88.9% of SHNA and 32.0% of SHTZ, showing higher sequence diversity than *B. lengau* from South African cheetahs (*Acinonyx jubatus*). In one SHTZ, a *Babesia vogeli*-like sequence was identified. Hepatozoon felis-like parasites were identified in 64.7% of BHNA, 36.8% of SHNA and 44.0% of SHTZ. Phylogenetic analysis placed the sequences outside the major *H. felis* cluster originating from wild and domestic felids. Filarioids were detected in 47.1% of BHNA, 47.4% of SHNA and 36.0% of SHTZ. Phylogenetic analysis revealed high genetic diversity and suggested the presence of several undescribed species. Co-infections were frequently detected in SHNA and BHNA (BHNA median 3 pathogens, range 1-4; SHNA median 3 pathogens, range 2-4) and significantly rarer in SHTZ (median 1, range 0-4, 9 individuals uninfected). **Conclusions:** The frequencies of all pathogens groups were high, and except for *Rickettsia*, multiple species and genotypes were identified for each pathogen group. Ecological conditions explained pathogen identity and diversity better than host taxonomy.



Phantom of the forest or successful citizen? Analysing how Northern Goshawks (Accipiter gentilis) cope with the urban environment

Merling de Chapa M, Courtiol A, Engler M, Giese L, Rutz C, Lakermann M, Müskens G, van der Horst Y, Zollinger R, Wirth H, Kenntner N, Krüger O, Chakarov N, Müller AK, Looft V, Grünkorn T, Hallau A, Altenkamp R, Krone O. (2020).

R Soc Open Sci 7:201356. doi: 10.1098/rsos.201356.

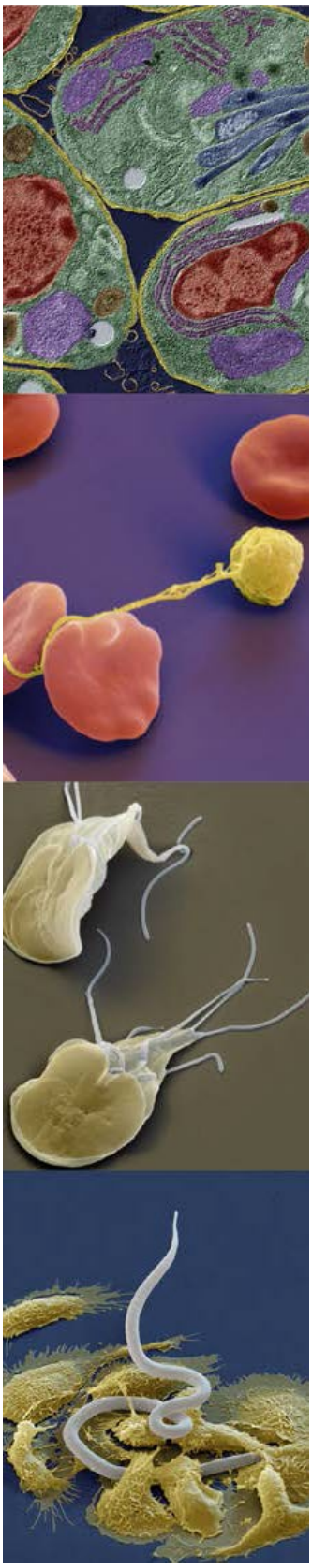
Abstract:
By 2040, roughly two-thirds of humanity are expected to live in urban areas. As cities expand, humans irreversibly transform natural ecosystems, creating both opportunities and challenges for wildlife. Here, we investigate how the Northern Goshawk (*Accipiter gentilis*) is adjusting to urban environments. We measured a variety of behavioural and ecological parameters in three urban and four rural study sites. City life appeared related to all parameters we measured. Urban female goshawks were overall 21.7 (CI95% 5.13-130) times more likely to defend their nestlings from humans than rural females. Urban goshawks were 3.64 (CI95% 2.05-6.66) times more likely to feed on pigeons and had diets exhibiting lower overall species richness and diversity. Urban females laid eggs 12.5 (CI95% 7.12-17.4) days earlier than rural individuals and were 2.22 (CI95% 0.984-4.73) times more likely to produce a brood of more than three nestlings. Nonetheless, urban goshawks suffered more from infections with the parasite *Trichomonas gallinae*, which was the second most common cause of mortality (14.6%), after collisions with windows (33.1%). In conclusion, although city life is associated with significant risks, goshawks appear to thrive in some urban environments, most likely as a result of high local availability of profitable pigeon prey. We conclude that the Northern Goshawk can be classified as an urban exploiter in parts of its distribution.

Increased immune marker variance in a population of invasive birds

Prüter H, Franz M, Twietmeyer S, Böhm N, Middendorff G, Portas R, Melzheimer J, Kolberg H, **von Samson-Himmelstjerna G**, Greenwood AD, Lüschow D, Mühldorfer K, **Czirják GÁ**. (2020).

Sci Rep 10:21764. doi: 10.1038/s41598-020-78427-7.

Abstract:
Immunity and parasites have been linked to the success of invasive species. Especially lower parasite burden in invasive populations has been suggested to enable a general downregulation of immune investment (Enemy Release and Evolution of Increased Competitive Ability Hypotheses). Simultaneously, keeping high immune competence towards potentially newly acquired parasites



in the invasive range is essential to allow population growth. To investigate the variation of immune effectors of invasive species, we compared the mean and variance of multiple immune effectors in the context of parasite prevalence in an invasive and a native Egyptian goose (*Alopochen aegyptiacus*) population. Three of ten immune effectors measured showed higher variance in the invasive population. Mean levels were higher in the invasive population for three effectors but lower for eosinophil granulocytes. Parasite prevalence depended on the parasite taxa investigated. We suggest that variation of specific immune effectors, which may be important for invasion success, may lead to higher variance and enable invasive species to reduce the overall physiological cost of immunity while maintaining the ability to efficiently defend against novel parasites encountered.