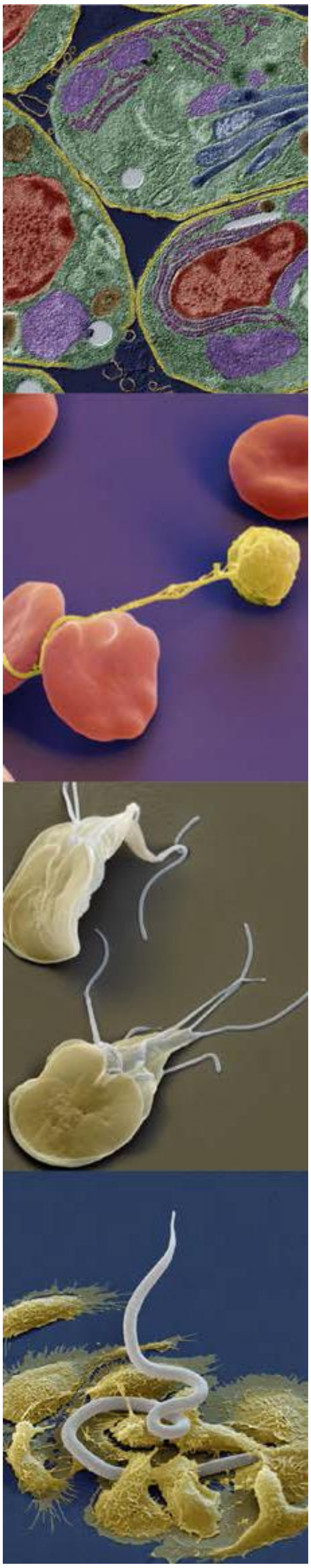
GRK 2046 Newsletter
April 2019



Summary, Update and News

Here, we bring you the 7th edition of our GRK 2046 newsletter. This is the first report after our evaluation in January 2019. In general, almost everybody had a good impression from these 2 days and all, first and second generation PhD students, did a pretty good job, thanks a lot! Most 1st generation students are busy now with writing, submitting or defending their thesis, if yet not already done. Meanwhile, we completed the recruiting of 2nd generation students with Felix and David. As usual, we report from recent travel with conferences/workshops and seminars/lectures. The Female Travel Award was awarded for research work in Africa, we give you the latest publications and a hint to upcoming seminars and talk. Enjoy!

– Marko Janke

New Students

David Holthaus

Hi all, I'm David. I did my Bachelor in Medical Biology and Master in Biomedical Sciences, both in Nijmegen, The Netherlands. During my masters I did two major internships with thesis, one about the influence of Interferon-stimulated gene 15 on virus susceptibility and resistance at the University of St. Andrews, Scotland, and the other about host responses to *G. Duodenalis* in organoid derived models at the Robert-Koch Institute here in Berlin. The last topic also covers my PhD project at the RKI in Toni Aebischer/Christian Klotz's group that aims at understanding the influence of *Giardia* on the human intestinal barrier. I try to characterize the model we have established in the previous generation and plan to make it more complex by introducing other factors such as different genetic makeup, like CF, secreted factors of other parasites, such as *Ascaris* spp., and/or immune cells.

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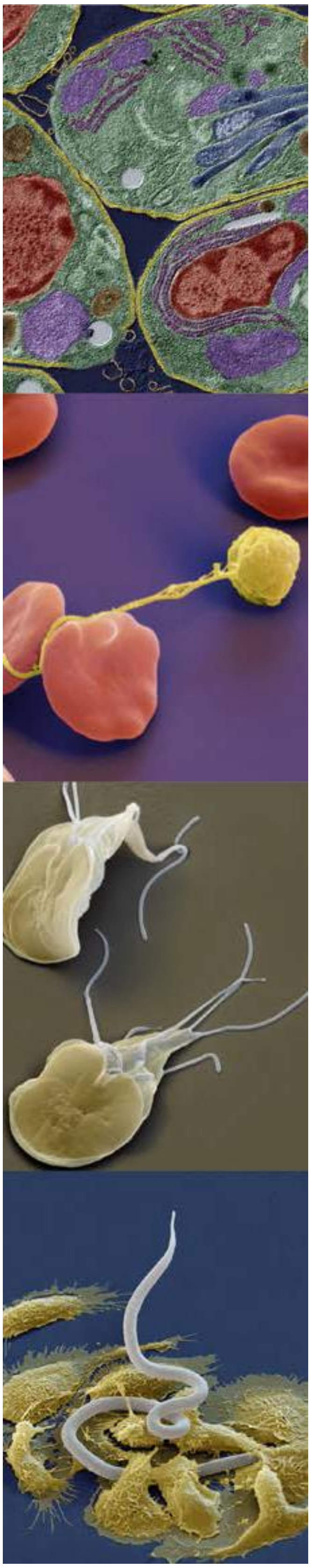

Felix Goerdeler

I completed both my BSc and MSc in Biochemistry at Freie Universität Berlin. After spending most of 2018 in Berkeley for a research semester, where I investigated the molecular basis of autophagy initiation using cryo electron microscopy, I submitted my master thesis last October. Since December, I am a PhD student at the Max Planck Institute of Colloids and Interfaces where I am working at the Biomolecular Systems department in the group of Prof. Peter Seeberger. The aim of my project is to characterize the biological role of glycosylations in *Plasmodium falciparum* communication via extracellular vesicles.

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Hongwei Zhang

I'm from China, I completed my BSc Biotechnology degree in Lanzhou University. Then I came to Beijing where I have completed my MSc Biology degree in Beijing Normal University in 2017. I came to Germany in September 2017 and carried out my PhD studies under the supervision of Prof. Dr. Susanne Hartmann and Dr. Sebastian Rausch at the Institute of Immunology, Department of Veterinary of Freie Universität Berlin. My research title is "Differential susceptibility to nematode infections is determined by the size of the parasite-specific type 2 T helper cell pool".

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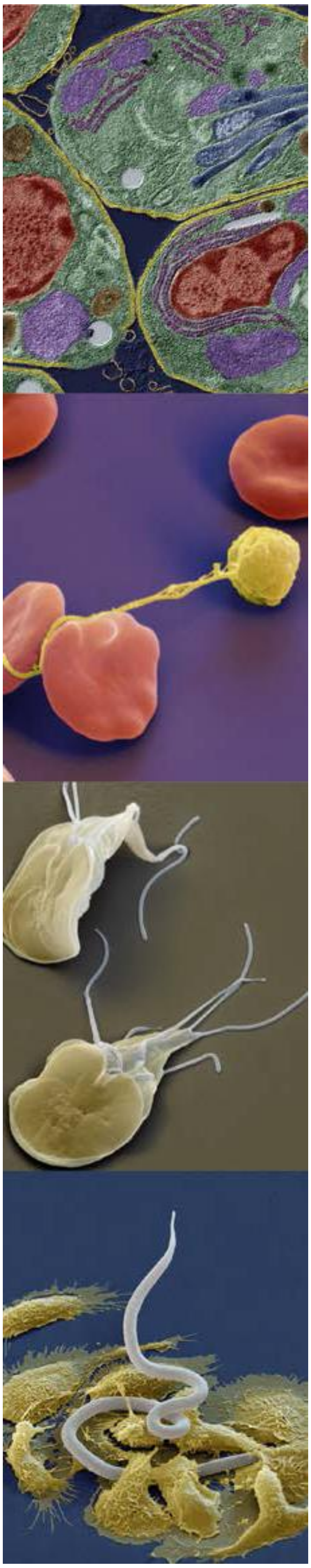

Sharareh Salehi

- I studied my Bachelor course in Medical Microbiology in Iran.
- I completed my Master degree in Molecular Biology and Biochemistry at Bonn University.
- Now I am a PhD Student at the Robert Koch-Institute under the supervision of Dr. Anton Aebischer. The title of my PhD project is: The Effect of Sphingolipid Derivatives on *Leishmania* Viability and Virulence.

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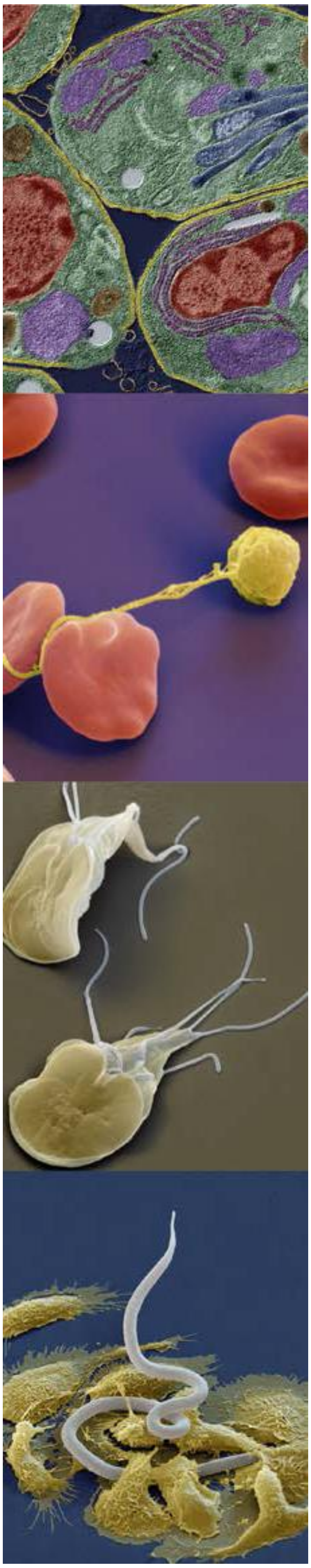
Travel & Conferences

Butare, Rwanda

In December, I joined our "international health research task-force" on a trip to Rwanda for one week. Prof. Mockenhaupt (my promotor) and two doctoral students of our group went there to set up the field-component of a study on the spread of anti-microbial resistance in Southern Rwanda. We plan to conduct a field-study on the presence of resistant *P. falciparum* strains in this region in the autumn of 2019 and this business trip was the perfect opportunity for me to meet my future colleagues and visit the collaborating health centres.

My week consisted of attending meetings with coordinating staff and visiting the medical/laboratory facilities of the university hospital in Butare, the district hospital in Kabutare and the medical health centre in Sovu. Since these facilities are relatively close to each other, our meeting-dense hours alternated with nice strolls from location to location, including selfie-moments with monkeys. This week was incredibly valuable for me with regard to the preparation and planning of our field- and lab work in the Butare region. Having the opportunity to meet all collaborators on forehand and taking advantage of the network that our research-group already has in Rwanda (thanks to Costanza Tacoli as well!) will save me a great deal of time and resources and truly feels as a privilege.

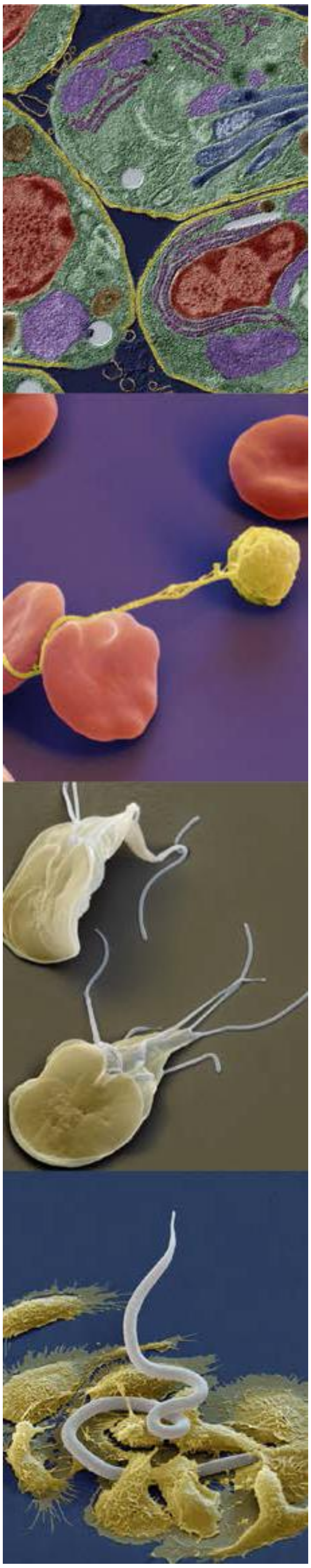


– Welmoed van Loon

DVG Fachtagung Parasitologie und Parasitäre Krankheiten

2-4 July 2018
Gießen, Germany

The DVG is held every year and attracts around 200 participants each time. The focus of this DVG was ‘New research results and current problems in practice’ and took place in the town of Gießen (Hessen, Germany). The DVG covers a broad range of topics from epidemiology, molecular mechanisms of parasite-host interactions, and anthelmintic resistance, to parasitic diseases in equids, zoo and wildlife animals. We really enjoyed this diverse spectrum of talks very much. Also during the poster session, we were able to see and discuss many interesting projects with other colleagues. We were able to collect ideas and to



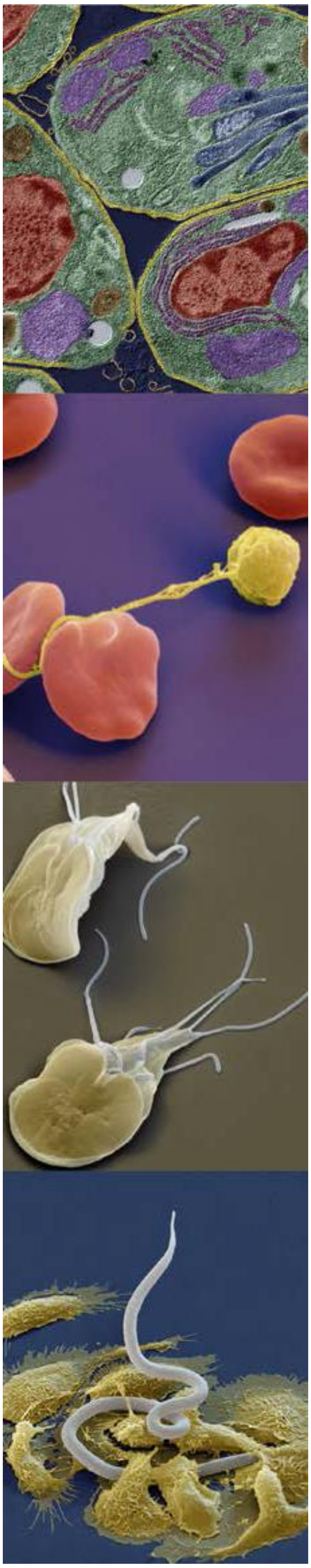
develop new approaches for our own projects. We have not yet been able to present a poster or talk at this conference, but with the new impressions and ideas, we may be looking forward to presenting our results at the next DVG conference. A highlight of this conference was the social evening sponsored by a big company, which allowed us to talk in a familiar setting to scientists in industry. Overall, the DVG was a great meeting in a familiar and friendly atmosphere, which we can recommend to everyone wanting to get an idea about the diverse research topics of parasitology.

– Irina Diekmann and Natalie Jakobs

Trends in Biodiversity and Evolution – Host-Parasite Interactions

6th – 7th December 2018
Vairão, Porto, Portugal

Trends in Biodiversity and Evolution (TiBE) is an annual meeting organized by the Research Centre in Biodiversity and Genetic Resources (CIBIO-InBIO), a research unit within the University of Porto addressing, among others, conservation and evolutionary genetics topics. This edition was dedicated to host-parasite interactions and speakers covered subjects including disease vectors, gut microbiome, climate modeling for prediction of disease spread & horizontal gene transfer. I presented preliminary results in a poster entitled “Immune responses to *Ancylostoma* in free ranging spotted hyenas” that provided a first chance to get feedback on a conference setting, for which I am grateful. It was rewarding meeting people passionate about working on autochthonous fauna and confirm that this is indeed one of the leading research institutes in this field in Portugal. The green urban surroundings and top quality food help making this conference even more recommendable. They also have a structured doctoral programme and obviously take postdocs, check out their website: https://cibio.up.pt/.



– Miguel Veiga

Serengeti Field Training Course, 2019

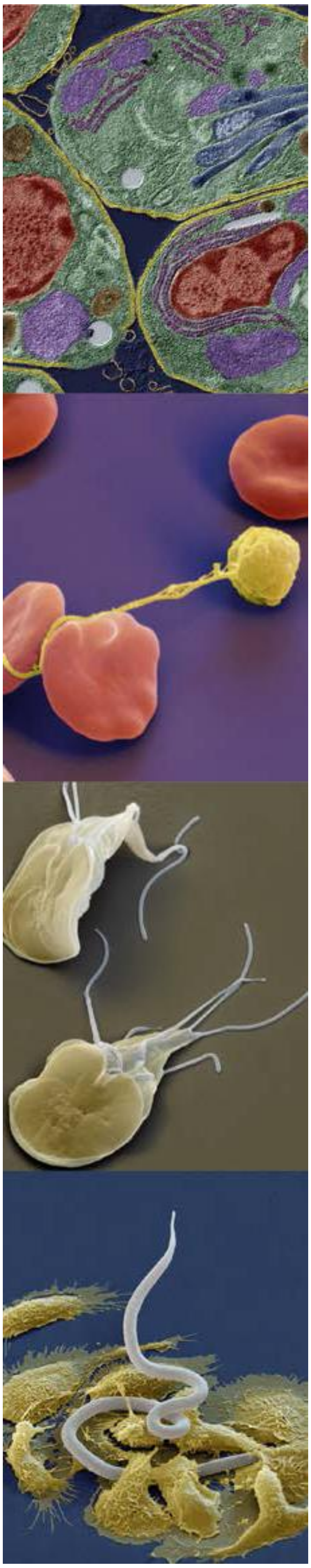
Participating GRK 2046 students and supervisors:

Alexander Gerhard, Ankur Midha, Benedikt Fabian, Benjamin Hamid, Irina Diekmann, Ivet Yordanova, Lubomír Bednář, Miguel Veiga, Prof. Emanuel Heitlinger, Prof. Georg von Samson-Himmelstjerna, Prof. Heribert Hofer, Prof. Marion East, Prof. Richard Lucius, Prof. Susanne Hartmann.

Summary

For the second time since the beginning of the GRK 2046, there was a chance for both students and supervisors to get some hands-on experience on sampling design and methodology in an unmanaged wildlife setting. In the Serengeti National Park (NP), Tanzania, animals embrace no other laws than the ones imposed by nature, meaning that addressing research questions requires a change in mindset comparing to what we are mostly used to.

We were based at the Serengeti Wildlife Research Centre (SWRC), about 15 km from the park headquarters in Seronera –> in the centre of



the Serengeti NP and accessible only by 12-passenger Cessna aircrafts. Since 1987, this is where the IZW spotted hyena project runs.

Our days were divided between: 1) going out in two 4x4 vehicles, guided by Marion, Heribert and Sonja, for hyena observation and samples collection (early morning & midafternoon) and 2) laboratory work. The projects focused on the study of parasite communities, mostly through non-invasive sampling, by gross and molecular parasite detection techniques.

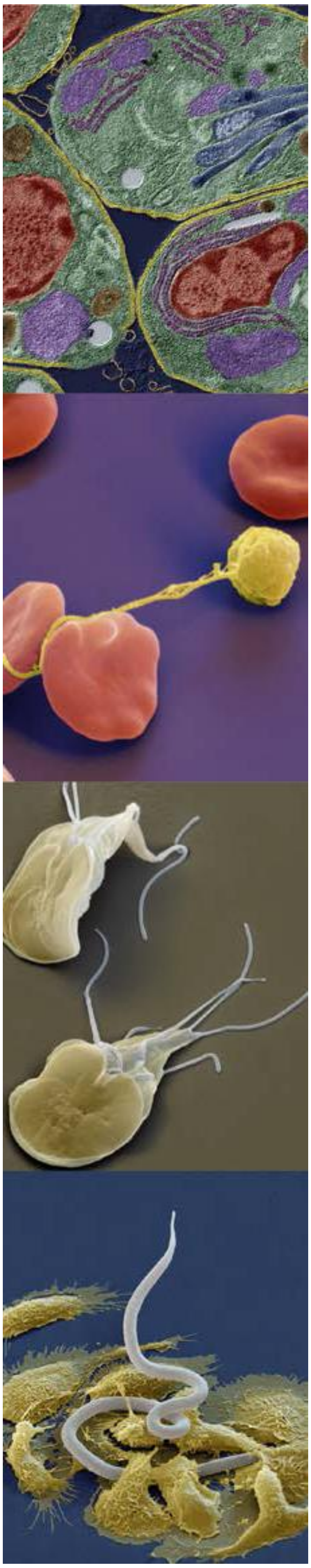
All of the students would like to thank the GRK 2046 and the participating PIs for funding and organising this incredible field training course. We will produce a separate booklet with much more information about the trip for those that are interested to read more.

– Miguel Veiga

Brief report on recent publication originating from the previous Serengeti field training course

As part of the Serengeti field training course, I had the opportunity to learn more about wildlife and non-invasive sampling. The Serengeti trip in 2016 led to the idea of using stool as a means to investigate gene expression. This then allowed the development of a non-invasive method that can be used to detect immunological changes in exfoliated cells found on the surface of stool. The use of this method has been developed and confirmed in a laboratory setting using the gastrointestinal nematode infection, *H. polygyrus*. A cysteine-rich cytokine that is involved in worm expulsion known as resistin-like molecule (RELM)-beta was detectable using exfoliated cells. This novel non-invasive technique has now been published in Frontiers in Immunology (Ahmed et al., 2019). Abstract shown below.

– Norus Ahmed



Berlin Parasitology Seminars (BPS)

Steffen Hahnel
Bayer Animal Health, Leverkusen

12th February 2019

Steffen Hahnel, currently working at Bayer Animal Health (Leverkusen), presented his work of his postdoctoral period in the lab of Eric Andersen of Northwestern University. His talk was entitled “Benzimidazole resistance in *C. elegans* wild isolates” and focused on the detection of natural occurring resistance against albendazole by genome-wide association mappings. In particular, he talked about the variation in the β-tubulin gene *ben-1* among wild *C. elegans* isolates from around the world and showed that resistance to ABZ naturally exists. Additional molecular analyses of various β-tubulin genes indicated that benzimidazole resistance in natural niches is a stronger selective pressure than the loss of one β-tubulin gen. The talk was followed by a lively discussion and an informal get together after the talk.

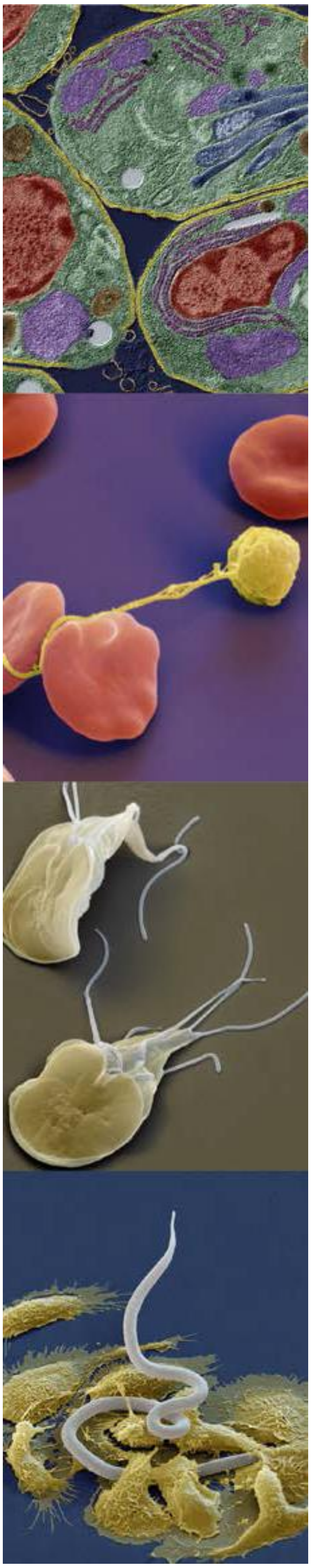
– Natalie Jakobs

Oliver Billker
Umeå University

11th December 2018

As the last BPS of the year I had the honor to host Prof. Oliver Billker. He recently moved to the Laboratory for Molecular Infection Medicine Sweden in Umeå University but since 2003 his research has been focused on molecular genetic in *Plasmodium* parasites. During his talk, he introduced us to the main outcome of the PlasmoGEM project, and how the generation of a barcoded library of DNA vectors that can be used to manipulate *Plasmodium* parasites and to screen for specific genes linked to the development of these organisms. Particularly, he remarked the screening of more than 3000 genes involved in sexual development due to their importance during the reproduction stages in mosquitos and during the transmission of *Plasmodium*.

Finally, Prof. Billker described the relevance of AP2-G2 as a repressor of transmission-specific genes during asexual stages (in blood) and sexual stages (gametocytes), and he define this protein as “master regulator” in *Plasmodium* development.



All the interesting and exciting information given during his talk highlighted the link of bioinformatic work to laboratory experiments and the successful outcome for studying the biology of parasites like *Plasmodium*.

– Victor Hugo Jarquín Diaz

Malcolm Kennedy
University of Glasgow

29th January 2019

For our first BPS of 2019 we had the pleasure of hosting Prof. Malcolm Kennedy who discussed a range of projects concerning nematode biology in a talk entitled “Adventures in parasitic nematodes: from immunogenetics to biophysics and protein structural biology”. As a Professor of Natural History, Prof. Kennedy’s research interests are compelling and diverse ranging from molecular and structural biology of proteins to the evolution of viviparity in mammals and nesting by marine turtles. As such, he gave us an overview of some of the many problems which he has worked on throughout his career including potential starting points for future work to be taken up by the next generation of parasitologists.

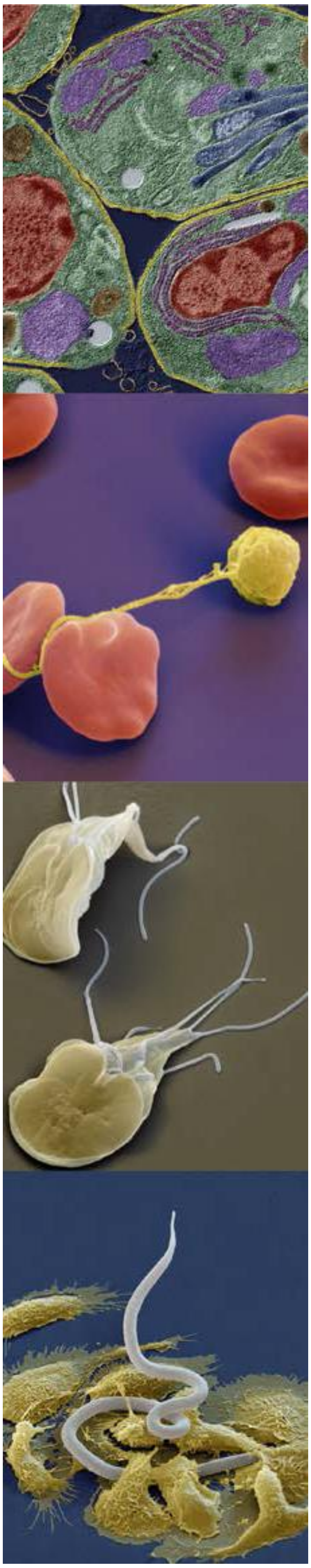
– Ankur Midha

Cinzia Cantacessi
University of Cambridge

12th March 2019

Dr. Cinzia Cantacessi is a Senior Lecturer in Parasitology in the Department of Veterinary Medicine where her group applies high-throughput sequencing technologies to study host-parasite interactions with an emphasis on soil-transmitted helminths of vertebrates. In a talk entitled “Is this gut big enough for the both of us? Exploring helminth-microbiota interactions in animal models and humans”, Dr. Cantacessi discussed potential therapeutic applications of helminth infections, including in clinical settings for patients suffering from chronic inflammatory diseases such as multiple sclerosis. The seminar was followed by a lively discussion.

– Ankur Midha



Role Models Seminars

Katharina Ribbeck
Massachusetts Institute of Technology

21st November 2018

Prof. Katharina Ribbeck at the Department of Biological Engineering, MIT, Boston gave her talk on "Finding a Niche: Microbial Colonization of Host Mucosal Barriers". Prof. Ribbeck investigates the role of intestinal and other mucus hydrogels as a protective barrier against pathogens such as parasites. Recently, she has gained increased interest in the signalling role that sugars in mucus may have on bacteria, which is an intiguing idea also for parasitologists. As a successful researcher and mother, Prof. Ribbeck serves as an excellent role model for PhD students and she shared her views on how to combine private life with a research career. I also received lots of unique input on future project ideas.

– Totta Ehret Kasemo

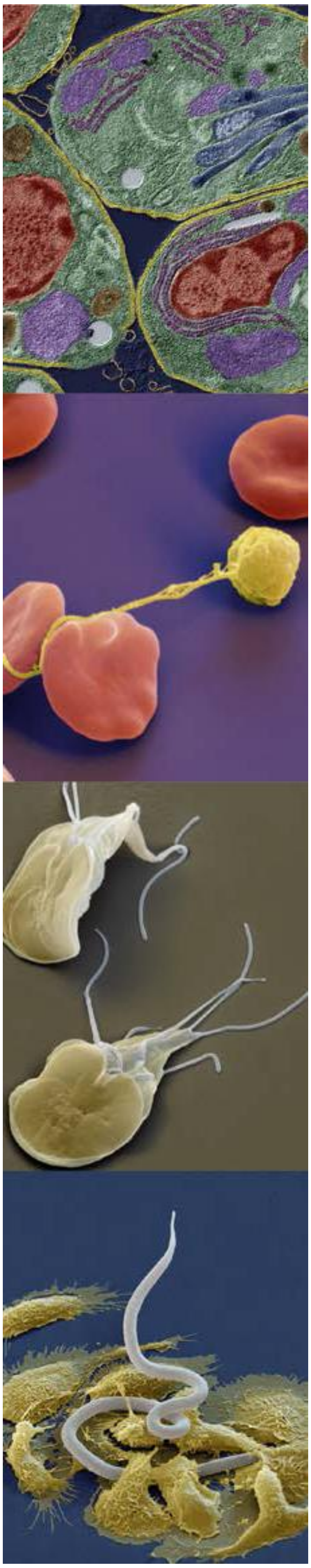
Faith Osier
Heidelberg University Hospital

27th November 2018

Prof. Faith Osier joined us for the last Role models seminar of 2018. In her talk titled “People versus Parasites: Learning to win against *Plasmodium falciparum*”, she discussed the work her lab is doing to identify new vaccine candidates for malaria. She discussed two strategies that her lab is pursuing 1) identification of surface antigens from the merozoite stage of *Plasmodium falciparum* and 2) identification of *Plasmodium* specific antibody responses from people who show natural immunity to *Plasmodium falciparum* malaria infection.

In addition to sharing her recent scientific findings she also discussed and shared her career journey and her personal experiences during the different stages of her career.

– Caroline Kiuru



Berlin Seminar for Resistance Research (BSfRR)

Erik Anderson
Northwestern University

11th December 2018

Erik Andersen presented his work on “Anthelmintic mechanisms of action and resistance from *C. elegans* natural diversity” within the framework of the Berlin Seminar for Resistance Research (BSfRR). The Andersen lab combines quantitative genetics (next-generation sequencing) with high-throughput phenotyping to answer questions about the adaptation of the free-living nematode *Caenorhabditis elegans* to its environment, also in the context of resistance. Using *C. elegans*, they investigate natural diversity in anthelmintic responses, in particular to benzimidazoles and avermectins.

The lively discussion about his outstanding research was continued over pretzels and beers and several Ph.D. students also had the opportunity to get to know him more closely over dinner.

– Alexander Gerhard

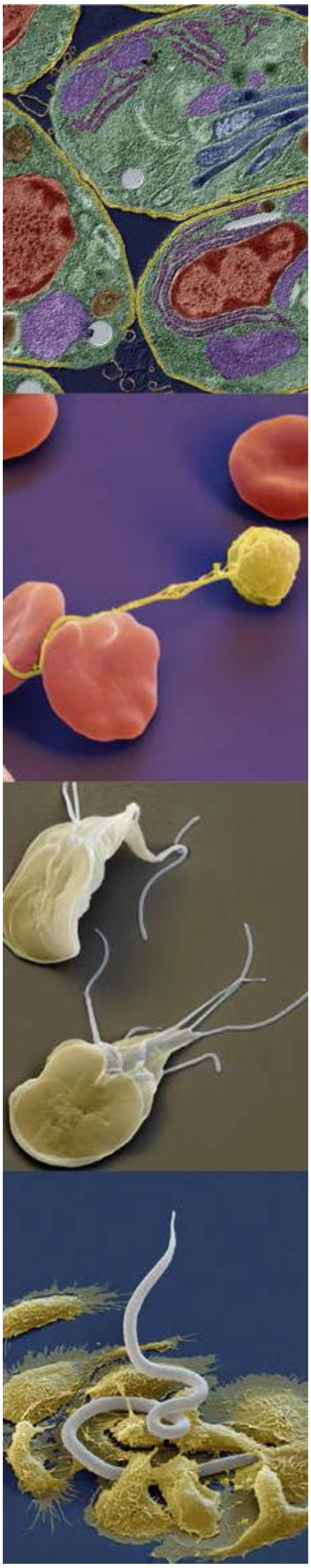
Upcoming Talks

BPS

30.04.2019, 17:00 – Tobias Steinfeldt – HGS (Mitte)
15.05.2019, 09:00 – Matthew Hepworth – VP (Düppel)
18.06.2019, 17:00 – Iain Wilson – RvO (Düppel)
09.07.2019, 17:00 – Holger Stark – VP (Düppel)
12.11.2019, 17:00 – Amy Buck – VP (Düppel)

Role Models

03.09.2019, 09:00 – Laura Knoll – HGS (Mitte)
01.10.2019, 09:00 – Malin Johansson – HU Parasitology (Mitte)
24.10.2019, 09:00 – Dragana Jankovic – VP (Düppel)



Publications

MiRNA-146a polymorphism increases the odds of malaria in pregnancy

Welmoed van Loon, Prabhanjan P. Gai, Lutz Hamann, George Bedu-Addo and Frank Mockenhaupt, 2019.

Malaria Journal, 18:7.

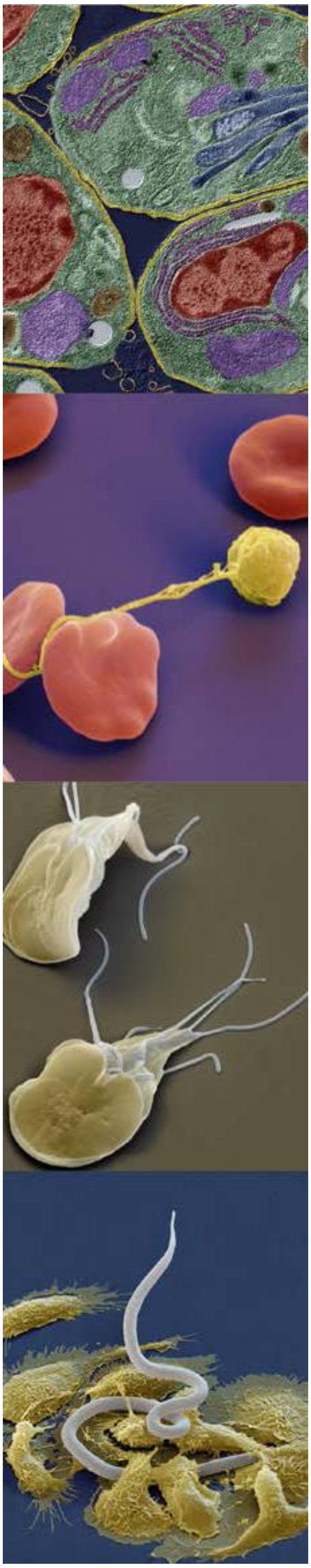
Abstract

Background: Plasmodium falciparum infection during pregnancy is a major cause of poor maternal health, adverse foetal outcome and infant mortality in sub-Saharan Africa. Genetic disposition is involved in susceptibility to malaria in pregnancy and its manifestation. MicroRNAs (miRNAs) influence gene regulation including that of innate immune responses. A miRNA-146a rs2910164 G > C single nucleotide polymorphism (SNP) has been associated with increased risks of several diseases, but no data as to malaria are available.

Methods: The association between miRNA-146a rs2910164 and P. falciparum infection among 509 Ghanaian women attending antenatal care (ANC) and 296 delivering Ghanaian primiparae was investigated. Malaria parasites were diagnosed by microscopy and PCR. Leukocyte associated hemozoin in placental samples was recorded as well. Proportions were compared between groups by Fisher's exact test, and logistic regression models were used to adjust for possible confounders.

Results: By PCR, P. falciparum infection was detected in 63% and 67% of ANC attendees and delivering primiparae, respectively. In both groups, two in three women were either heterozygous or homozygous for miRNA-146a rs2910164. Among ANC attendees, homozygosity conferred increased odds of infection (adjusted odds ratio (aOR), 2.3; 95% CI, 1.3–4.0), which was pronounced among primigravidae (aOR, 5.8; 95% CI, 1.6–26) but only marginal in multigravidae. Likewise, homozygosity for miRNA-146a rs2910164 in primiparae increased the odds of past or present placental P. falciparum infection almost six-fold (aOR, 5.9; 95% CI, 2.1–18).

Conclusions: These results indicate that SNP rs2910164 G > C is associated with increased odds for P. falciparum infection in first-time pregnant women who are considered to lack sufficient acquired immune responses against pregnancy-specific strains of P. falciparum. These



findings suggest that miRNA-146a is involved in protective malarial immunity, and specifically in the innate component.

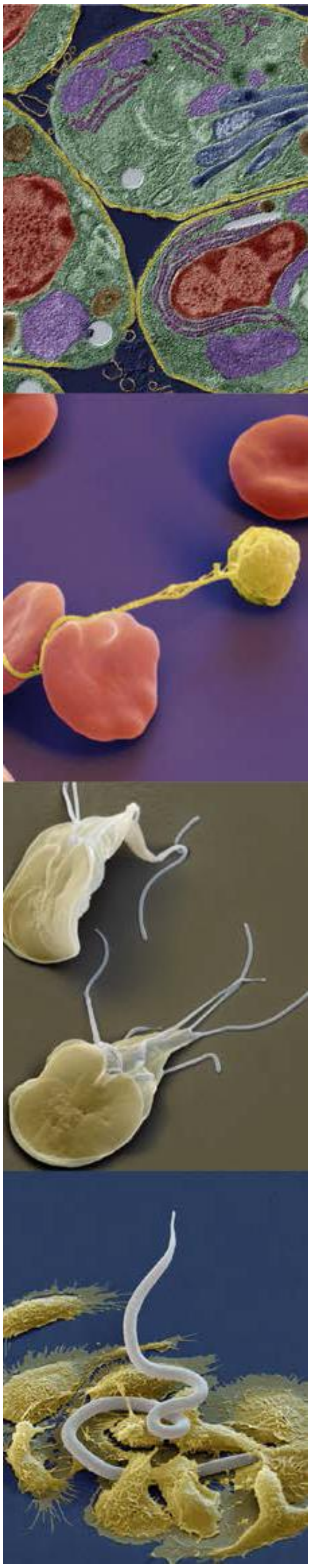
Concurrent proteomic fingerprinting and molecular analysis of cyathostomins

Christina Maria Bredtmann, Jürgen Krücken, Jayaseelan Murugaiyan, Alice Balard, Heribert Hofer, Tetiana A. Kuzmina and Georg von Samson-Himmelstjerna, 2019.

Proteomics, 19:e1800290.

Abstract

Rapid, cost-effective, efficient and reliable helminth species identification is of considerable importance to understand host-parasite interactions, clinical disease and drug resistance. Cyathostomins (Nematoda: Strongylidae) are considered to be the most important equine parasites, yet research on this group has been hampered by the large number of 50 morphologically differentiated species, their occurrence in mixed infections with up to 15 species and the difficulties associated with conventional identification methods. Here, MALDI-TOF MS, previously successfully applied to identify numerous organisms, was evaluated and compared with conventional and molecular genetic approaches. A simple and robust protocol for protein extraction and subsequent DNA isolation allowing molecular confirmation of proteomic findings was developed, showing that MALDI-TOF MS can discriminate adult stages of the two closely related cyathostomin species *Cylicostephanus longibursatus* and *Cylicostephanus minutus.* Intraspecific variability of proteomic profiles within morphospecies demonstrated an identification of morphospecies with an accuracy of close to 100%. In contrast, three genospecies within *C. minutus* and sex-specific profiles within both morphospecies could not be reliably discriminated using MALDI-TOF MS. In conclusion, MALDI-TOF MS complemented by the novel molecular protocol is a reliable and efficient approach for cyathostomin species identification.



From entry to early dissemination – *Toxoplasma gondii*'s initial encounter with its host

Estefania Delgado Betancourt, Benjamin Hamid, Benedikt T. Fabian, Christian Klotz, Susanne Hartmann and Frank Seeber, 2019.

Frontiers in Cellular and Infection Microbiology, 9:46.

Abstract

Toxoplasma gondii is a zoonotic intracellular parasite, able to infect any warm-blooded animal via ingestion of infective stages, either contained in tissue cysts or oocysts released into the environment. While immune responses during infection are well-studied, there is still limited knowledge about the very early infection events in the gut tissue after infection via the oral route. Here we briefly discuss differences in host-specific responses following infection with oocyst-derived sporozoites vs. tissue cyst-derived bradyzoites. A focus is given to innate intestinal defense mechanisms and early immune cell events that precede *T. gondii*'s dissemination in the host. We propose stem cell-derived intestinal organoids as a model to study early events of natural host-pathogen interaction. These offer several advantages such as live cell imaging and transcriptomic profiling of the earliest invasion processes. We additionally highlight the necessity of an appropriate large animal model reflecting human infection more closely than conventional infection models, to study the roles of dendritic cells and macrophages during early infection.

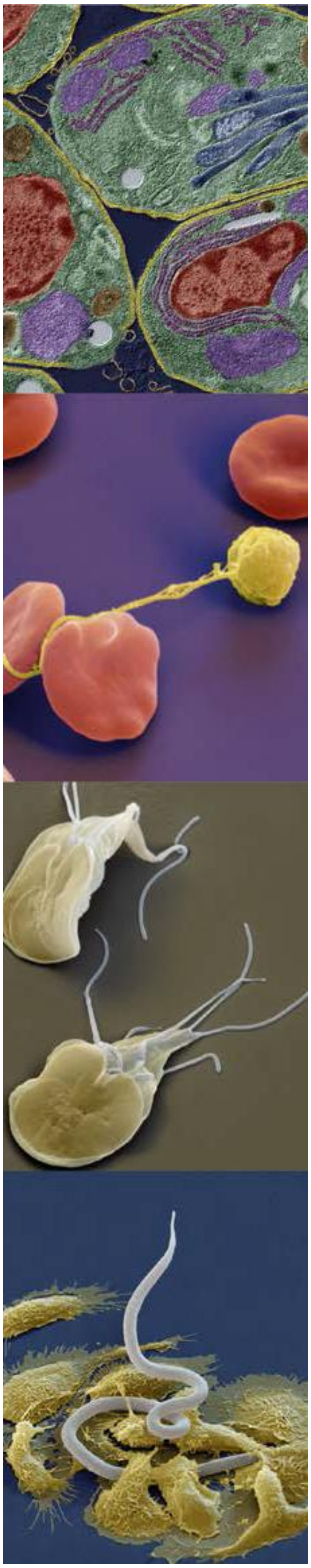
A novel non-invasive method to detect RELM beta transcript in gut barrier related changes during a gastrointestinal nematode infection

Norus Ahmed, Emanuel Heitlinger, Nicole Affinass, Anja A. Kühl, Natasa Xenophontos, Victor Hugo Jarquin, Jenny Jost, Svenja Steinfelder and Susanne Hartmann, 2019.

Frontiers in Cellular and Infection Microbiology, 10:445.

Abstract

Currently, methods for monitoring changes of gut barrier integrity and the associated immune response via non-invasive means are limited. Therefore, we aimed to develop a novel non-invasive technique to investigate immunological host responses representing gut barrier



changes in response to infection. We identified the mucous layer on feces from mice to be mainly composed of exfoliated intestinal epithelial cells. Expression of RELM-β, a gene prominently expressed in intestinal nematode infections, was used as an indicator of intestinal cellular barrier changes to infection. RELM-β was detected as early as 6 days post-infection (dpi) in exfoliated epithelial cells. Interestingly, RELM-β expression also mirrored the quality of the immune response, with higher amounts being detectable in a secondary infection and in high dose nematode infection in laboratory mice. This technique was also applicable to captured worm-infected wild house mice. We have therefore developed a novel non-invasive method reflecting gut barrier changes associated with alterations in cellular responses to a gastrointestinal nematode infection.

Evaluation

On January 9-10, 2019, all minds were concentrated on the On-Site visit of reviewers and representatives of the DFG and the Berlin Senate, taking place in the Veterinarium Progressum, Oertzenweg 19b, Frei Universität. Our guests arrived on January 9 after lunch and first held a short internal briefing. Afterwards, the speaker and four representative PhD students presented our RTG and their own projects. This oral talk session was followed by the general poster session, where all PhD students explained their projects to the reviewer. However, one of the highlights was certainly the discussion between reviewers and PhD students, PIs excluded! After a “resting” night, the second day brought first, the overall discussion for all RTG members followed by the final internal briefing of our guest. As a result, we got happy news that our RTG is considered to get further funding. However, the final vote whether we get funded for a second period is made in May, 2019. We all keep our fingers crossed!

It remains only to thank all the people who helped in prepairing, organising and holding the evaluation. Not only all PhD students and PIs. But, a special THANK YOU to all technicians of the Hartmann group and the immunology secretariat (FUB) for providing endless delicious food and helping with organising, arranging and designed. Wouldn’t have been possible without so many helping hands!

– Marko Janke