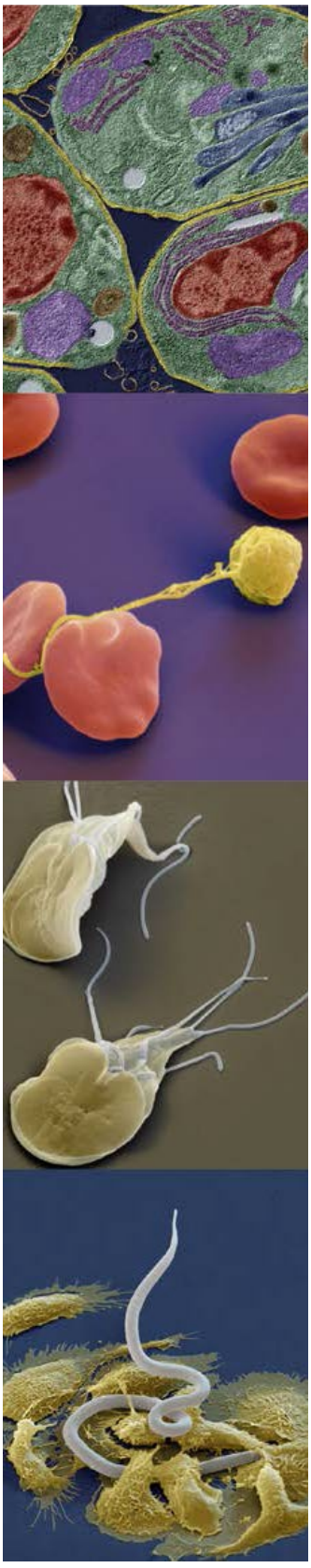
GRK 2046 Newsletter
June 2023



Summary, Update and News

Dear,
Sadly, we are speeding up towards the completion of our Research Training Group in 2024. Our third generation PhD students taking the opportunity to attend useful workshops for getting funding, career advices, and also soft skills. One highlight during the first half year in 2023 was definitely our Africa workshop “Field work” in Namibia, where PhD students learned how to prepare and conduct field work, including how to acquire samples from wild anmals. For this, all students developed small own projects in analyzing samples taken from wild animals. Upon arrival, we set a base lab at Okambara Lodge. No matter if weekend, late or early in the morning, our PhD students enthusiastically collected samples and analyzed them. Regular team meetings after Dinner were taking place to prepare the next day. On this, and much more we report in this newsletter edition, edited by Lilla.

Have fun!

- Marko

Conferences

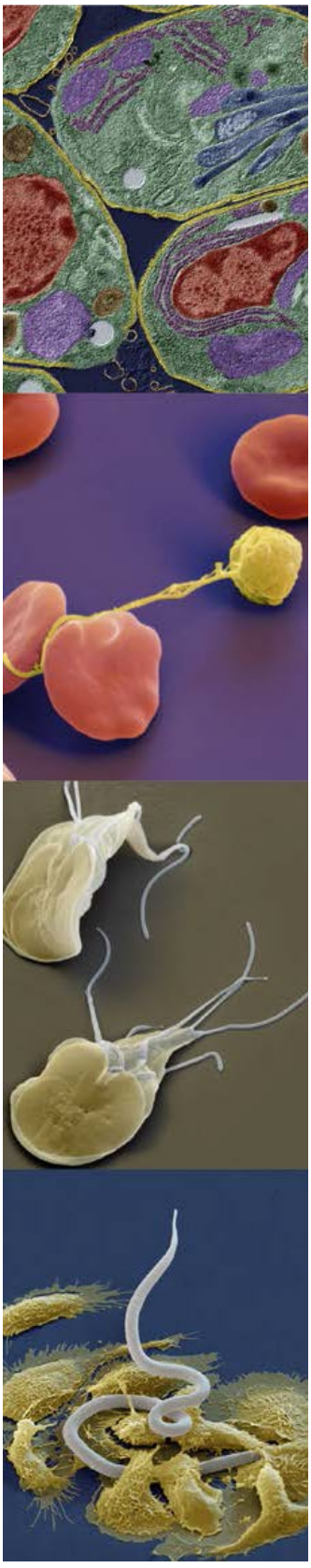
Global Virtual Symposium on Toxoplasmosis

January 23-24, 2023, Virtual

taken from:
https://unitedscientificgroup.com/conferences/toxo-2023/

In January, I participated at the Global Virtual Symposium on Toxplasmosis (TOXO-2023). The symposium was held for the 3rd time and offered a rich program of presentations on toxoplasmosis research. All of the talks were very informative and many new exciting results were shared. This virtual symposium series was launched during the COVID pandemic, and while it offers limited networking opportunities compared to in person meetings such as the Toxo conference every other year, I hope this format continues in addition as it conveniently brings together many great speakers from around the world. In summary, the two days were very educational and I gained many new inspirations for my own research.

- David Warschkau (Project C3)



DGP Meeting

March 15-17, 2023, Gießen (Germany)

taken from: https//parasitology-meeting.de

Photo by Ricarda Leisering

In March, I was able to attend the 30th annual meeting of the German Society for Parasitology (DGP), which was hosted at the Campus for Law and Economics of the Justus-Liebig-University in Gießen. Since our graduate school unites doctoral researchers of different institutes in their ambition to explore various aspects of parasitic life, attendance of a parasitology-themed conference was a natural fit.

The program offered talks, posters and workshops on a vast range of different parasites in parallel sessions, with nine keynote lectures ranging from protozoan to metazoan infections of humans and animals. Next to the workshop on the importance of the liver as a gatekeeper in parasitic invasion processes organized by students of our own graduate school, I specifically enjoyed the keynote lecture given by Dr Staffan Svärd talking about the influence of parasite fitness on host epithelial responses. The topic of his research using organoid models in context of *Giardia* infection nicely matched my own, which I was able to present on the last day of the conference.

After years of canceled, postponed, online-attendance or Berlin-based meetings due to pandemic restrictions, it felt like the first “real” conference for many PhD students of the final GRK 2046 generation. It was a pleasure to get a glimpse of research life in pre-pandemic times and I am therefore hoping to attend many more in person conferences in the future to connect with other researchers on a scientific and personal level.

- Antonia Müller (Project B3)

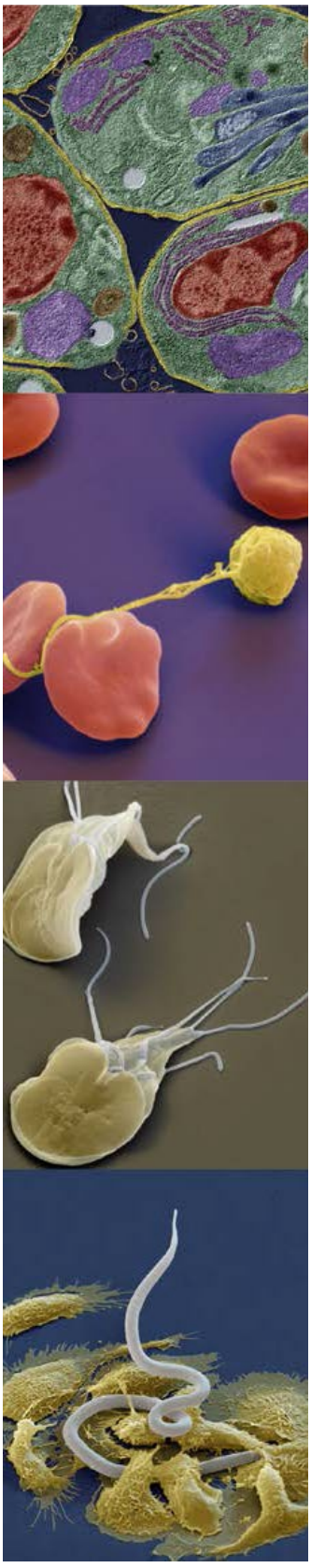


Photo by Antonia Müller

In March, the 30th Annual Meeting of the German Society for Parasitology was held in Gießen, Germany. It was done in person; a break from the virtual / hybrid events after the Covid19 pandemic. My colleague, Susana Soares, and I were tasked in organizing the 90minute-GRK 2046 workshop for the conference. Our workshop was centered around the liver; titled “Liver: gatekeeper for parasite invasion?”. The main goal of the workshop was to represent all / various parasites that reside or pass through the liver. Not only were the parasites represented, but also various techniques used to understand the parasites and their effects on the host were displayed; from proteomics to spatial transcriptomics. As our keynote speaker, Dr Katrin Neumann gave insight into the general importance of the liver with regard to immunology, providing a possible explanation as to why the parasites pass through it; due to its immunotolerance nature.

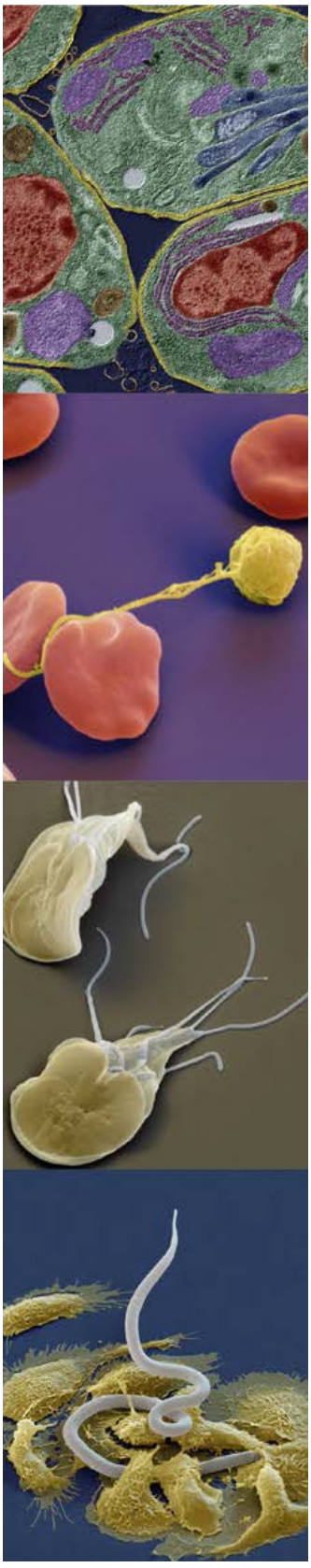
- Zaneta Kidiavai (Project B4 associated)

15th Malaria Meeting

March 23-24, 2023, Hamburg (Germany)

I attended the 15th Malaria meeting from the 23rd to the 24th of March in Hamburg. Our host was the Bernhard Nocht Institute this year. It was my first time to attend a malaria-specific meeting, and it did feel very different in a good way! It has developed into an event where both, clinicians and natural scientists share their research even beyond the border of Germany. During this short yet full schedule of a 2-day meeting, many topics from clinical research to immunology and molecular parasitology were covered. I even made some new connections in the poster session - it was amazing! Unfortunately, the malaria meeting happens every other year, so it is my first and probably last time I attend during my PhD student time, but like the keynote speaker - Prof Faith Osier from Imperial College London said, it will be very exciting to see more fantastic female researchers as keynote speaker next time.

- Tinghuan Song (Project B1)



10th *Encontro de Formação da Ordem dos Médicos Veterinários* (EFOMV)

April 14-16, 2023, Lisbon (Portugal)

taken from https://www.efomv.pt/

On these days, I got the opportunity to return home, because I was invited to present a poster on “Long term effects: intestinal parasitism and immunosenescence in wild spotted hyenas” in the 10th Training Meeting of the Order of Veterinary Doctors organized with the high patronage of the President of the Portuguese Republic.

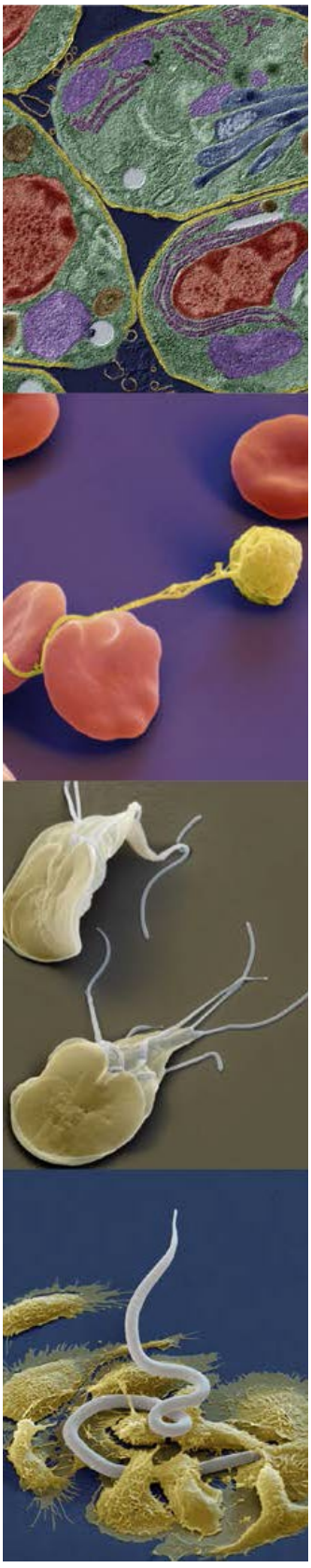
This event, although recent, has become one of the most important in my country. It represents the moment where we, Portuguese vets:

- meet our old friends;
- make new connections with the new generations of veterinarians;
- check where in the world and on what everyone is working;
- update our current knowledge in a lot of different areas with renowned national and international colleagues;
- debate on problems inherent to our profession, look for solutions and discuss its future.

Photos by Susana Soares

This year, we also had the pleasure to welcome colleagues from Africa and their Order´s representative, which further increased the value of such an opportunity.

Because of COVID, the meeting was canceled several times, given that everyone either was forced to change their workflows or was shortlisted to help other health professionals to control the transmission chains, contain the waves and deal with the aftermath, like myself. Only now,



everything has returned to a more peaceful pace - within the normal hectic life style that we are already too familiar with…. and in a way, everyone was really looking forward to attend this event!!! Who can say no to such a pleasant place, as close to the river Tejo as possible, and with summer-like weather!

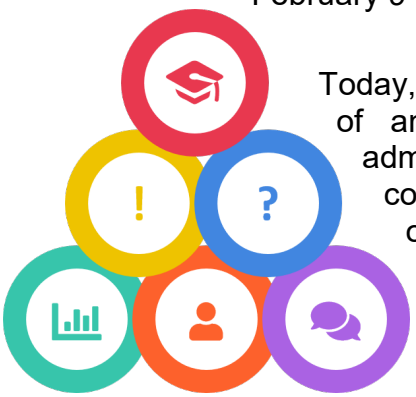
Although the section on wildlife is still a little under-represented, having this chance to be there and showcase what I am doing, allowed me to get a more practical point of view of what vets could be expecting from such a topic and raise their interests in such kind of studies. So, next year I am expected to be there again with new developments!

- Susana Soares (Project C4)

Workshops / Courses

Basics of business administration

February 9-10, 2023 (DRS, Dr Alexander Egeling)



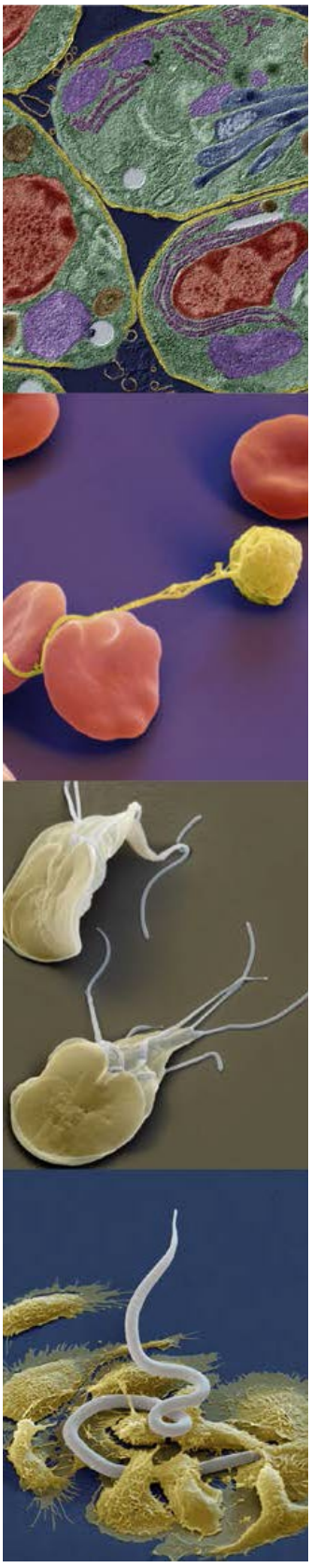
Taken from:
https//www.alexander-egeling.de

Today, I would like to provide you with an overview of an online beginner's course in business administration that I recently attended. The course, led by instructor Alexander Egeling, offered a comprehensive introduction to the field, equipping participants with essential knowledge and insights.

The online format of the course allowed for flexible engagement with the material at our own convenience. Through well-structured modules, we were introduced to fundamental concepts and principles in business administration, covering a range of topics including finance, marketing, operations, and strategic management.

One notable aspect of the course was its emphasis on practical application. Alexander Egeling effectively incorporated real-world examples and case studies to illustrate the practical implementation of business theories. This approach enhanced our understanding of the subject matter and its relevance in real business contexts.

Alexander Egeling demonstrated expertise and a passion for the subject matter as an instructor. He provided concise explanations and was readily available to address questions and offer guidance. Despite the



online nature of the course, he fostered a supportive learning environment, encouraging active participation and facilitating engaging discussions among participants.

The course also offered opportunities for interaction and collaboration through online forums and virtual group projects. These activities allowed participants to exchange ideas, share perspectives, and learn from each other's experiences, enriching the learning process and enabling a deeper exploration of business concepts.

Upon completing the course, I gained a solid foundation in business administration. The knowledge and insights acquired have broadened my understanding of business operations and strategic decision-making. Whether pursuing a career in industry or furthering academic studies, the course has provided valuable insights applicable to various professional settings.

In conclusion, the online beginner's course in business administration, led by instructor Alexander Egeling, offered a well-structured and comprehensive introduction to the field. The practical focus, combined with interactive elements and expert guidance, made it a valuable learning experience. I would recommend this course to those seeking to develop a foundational understanding of business administration.

- Grace Klass (Project C5)

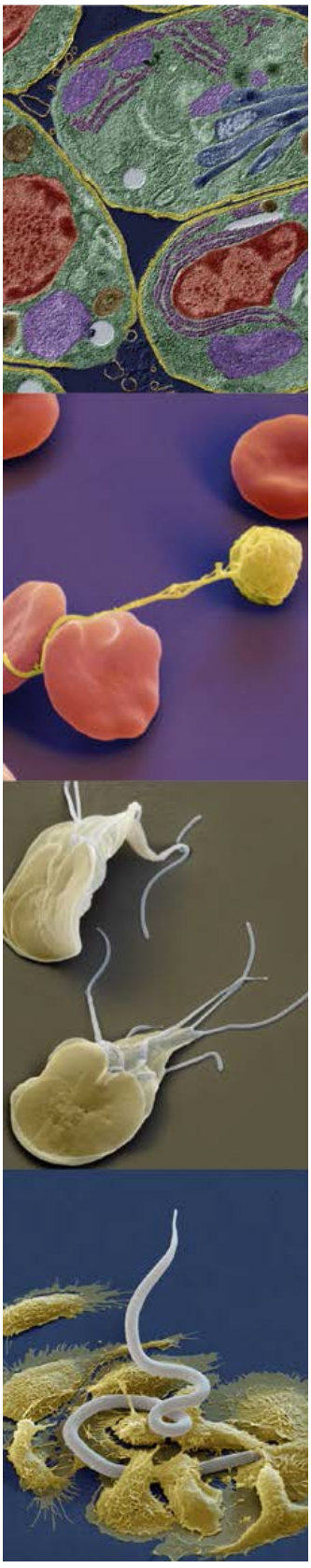
From Biology to Mathematics: adding precision and predictive power to descriptive models

February 27 – March 3, 2023 (ZIBI, Prof Leonie Ringrose)

At the end of February, I participated in a 5-day workshop led by Prof Leonie Ringrose from the Humboldt University. As the title of the workshop suggests, Prof Ringrose took great effort to introduce us to dynamic models and show us how the potentially intimidating world of mathematical models and differential equations can be morphed into biologically relevant and useful models of various processes.

The workshop covered the whole process of model building: from a cartoonish representation of a biological phenomenon, through kinetic diagrams, differential equations, and Python programming, all the way to parameter scanning and model analysis.

Taken from https//science-kitchen.net



The mornings were spent in a more traditional lecture-type setting, while the afternoons were spent on individual work. Before the workshop, we were all asked to think about a biological process that we would like to model, and during the open afternoon sessions Prof Ringrose helped each of us in developing our own models. Her enthusiasm and dedication motivated all of us to spend as much time as we could thinking about and refining our models, which allowed us to have a presentation session on the final day. Here, we all presented the models we came up with in the previous 4 days, and we could all discuss together which directions it could still be improved.

As a result of Prof Ringrose's engaging personality and true investment into the course, we all managed to code and develop at least a starter version of dynamic model that we can later use for our projects. During these five days we were provided with helpful scripts that enabled even the least Python-proficient participants to develop a meaningful model, and along with the accompanying handbook and the afternoon sessions we made quite impressive progress. To anyone interested in understanding how mathematical modeling can add to their research, I can highly recommend this workshop.

- Lilla Jordán (Project C1)

Paid to research: preparing successful funding applications

March 6-7, 2023 (DRS, Matteo Garavoglia)

Taken from https://www.impulsplus.com

As researchers, we depend on funding to materialize our ideas and test out our hypothesis. As PhD students, we have our supervisors' grants however, if one is to stick to the non-industry path, one requires a skill in preparing successful funding applications. Matteo was able to provide insight on the "do's" and "don'ts" of funding applications, key emphasis on timelines (start the application process a year in advance), what to do after a rejection as well as identification of the right funders. On the second day of the workshop, we each had a one-on-one with him where we discussed personal prospects and went through applications (for those who had started on some).

- Zaneta Kidiavai (Project B4 associated)

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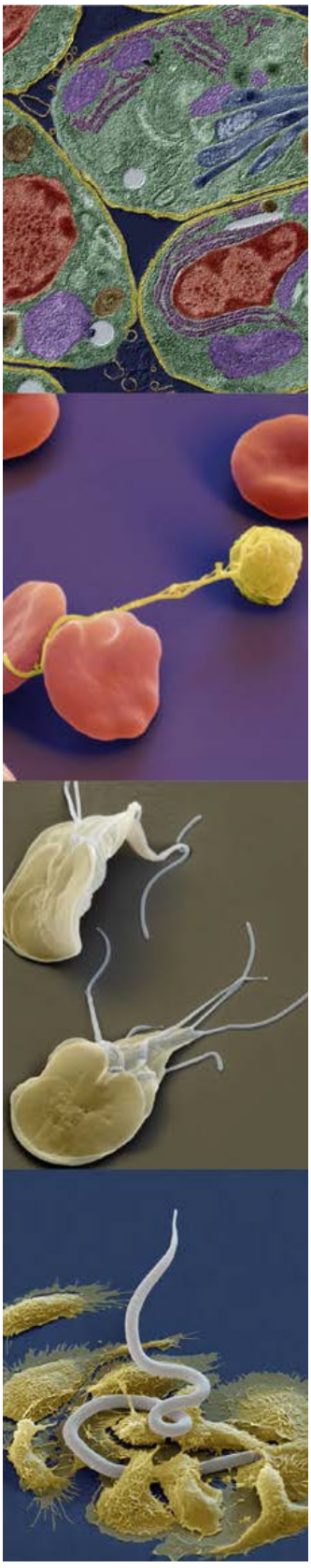


Scientific argumentation

March 2-3, 2023 (DRS, Kai Hüwelmeyer)

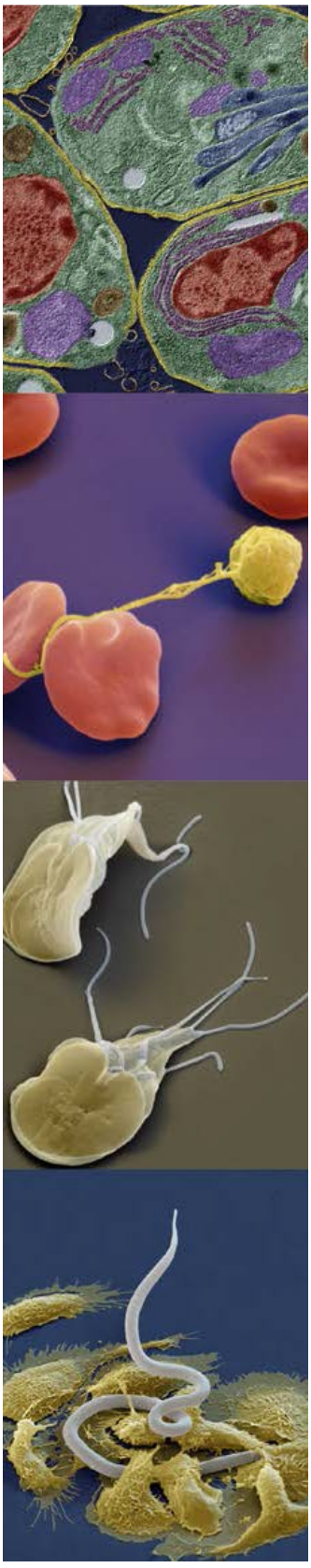
The workshop on "Scientific Argumentation" aimed to enhance participants' understanding and skills in constructing effective arguments within a scientific context. The workshop spanned over two days, featuring a variety of interactive sessions, group activities, and expert-led discussions. This evaluation offers a neutral assessment of the workshop, taking into consideration its organization, content, and overall effectiveness.

In terms of organization, the workshop was well-planned and executed. The schedule allowed for a balanced mix of theoretical presentations and practical exercises, providing participants with ample opportunities to apply the concepts learned. The facilitators were knowledgeable and well-prepared, ensuring a smooth flow of information throughout the workshop. The venue and logistics were also commendable, with appropriate facilities and resources readily available.

Regarding the content, the workshop covered a wide range of topics related to scientific argumentation. It explored fundamental principles such as logical reasoning, evidence evaluation, and counter-arguments. The presentations were clear, concise, and supported by relevant examples. However, some participants expressed the desire for more in-depth discussions and advanced techniques, as the content primarily catered to a beginner-to-intermediate level of understanding. A greater emphasis on complex case studies or real-world applications could have further enriched the content.

Taken from https://www.cartoonstock.com

The workshop's effectiveness varied among participants. For individuals new to scientific argumentation, the workshop provided a solid foundation and practical guidance. The interactive nature of the sessions encouraged active engagement and collaborative learning, fostering a positive learning environment. However, participants with prior experience in the field may have found certain parts repetitive or lacking in novel insights. While the workshop effectively addressed the basics, it could have benefited from incorporating advanced techniques to accommodate a wider range of skill levels. In terms of improvements, incorporating more interactive group activities and case studies involving real-world scientific controversies could enhance participant engagement. Additionally, providing supplementary materials or resources for further self-study would be beneficial for participants to continue their learning



beyond the workshop. Overall, the workshop on "Scientific Argumentation" successfully introduced participants to key principles and practices of constructing persuasive arguments within a scientific framework. While it may have been more suitable for beginners, it laid a solid foundation for participants to further develop their skills in scientific argumentation. With some adjustments to accommodate different skill levels and incorporate more advanced concepts, this workshop could effectively cater to a broader audience seeking to refine their scientific argumentation abilities.

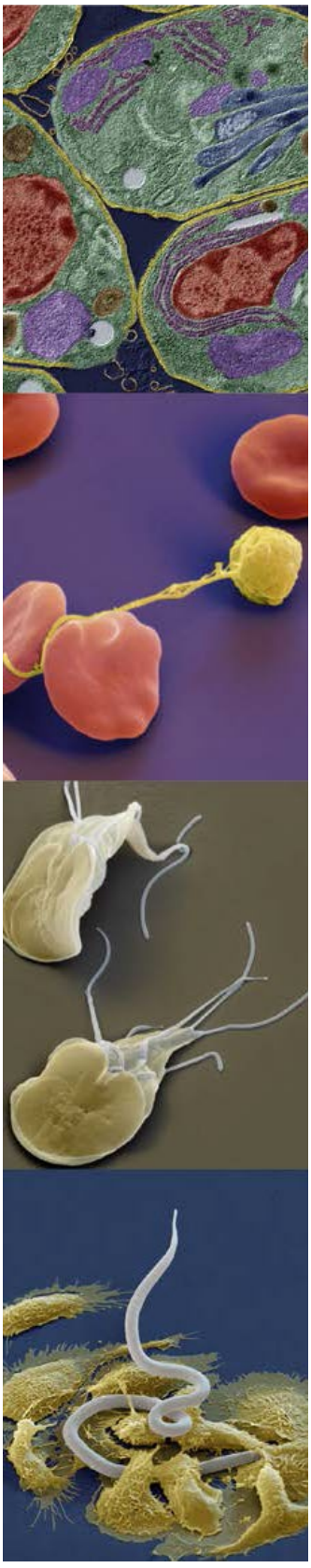
- Arkadi Kundik (Project B4 associated)

Disputationstraining

March 16-17, 2023 (HGS, Torsten Rother)

From 16th to 17th March 2023, I was attending the online course “Disputationstraining” led by Torsten Rother. Topics of the course included e.g. preparation of the oral part of the defence of doctoral thesis, time- and self-management during preparation phase and handling of exam anxiety and stage fright. The participants learned a lot of tools and techniques on how it is possible to stay confident and concentrated when confronted with tricky or provocative questions. The biggest advantage of this course was that all attending PhD students got the possibility to present a ‘mini’ doctoral defence within 5 minutes and Torsten and the other attendees formed an examination board that asked questions, afterwards. Thereby, we got the chance to apply the freshly learned tools on handling questions. Moreover, we got a very personal and helpful feedback on our presentation style and competence in answering questions from the examination board. Since the attending PhD students had highly different research backgrounds (e.g. law, psychology, visual arts) it was very interesting to learn about the various requirements and standards in their particular subject area. With his friendly and well-adjusted character, Torsten created a relaxed and trusting atmosphere that made it easy to talk honestly about concerns and insecurities when preparing for the final day. I would definitely recommend this course. The course language was German, but if you interested in attending, I am sure that is possible to contact Torsten Rother and find a solution.

- Maria Serocki (Project C1)



FACS course

April 24-25, 2023 (ZIBI / DRFZ, Toralf Roch, Hyun-Dong Chang)

On April 24th and 25th, I took part in the FACS Course organized by the Leibniz Graduate School on Chronic Inflammation. It was in person at the Deutsches Rheuma-Forschungszentrum (DRFZ) facility. The course involved an introduction into the principles of flow cytometry, which I found really enriching, as clear examples given by the lecturers were helpful to understand the sometimes-confusing terms used around this method of analyzing cells. Following the introduction, we could be part of practical sessions, which aim was to understand the handling of the different instruments used in flow cytometry. I really recommend this course for flow cytometry beginners and to people who have experience with the technique. Experts at DRFZ FACS facility are open to hear your questions and explain very simply the tips and tricks behind setting a panel, acquiring properly the cells and analyzing correctly your data.

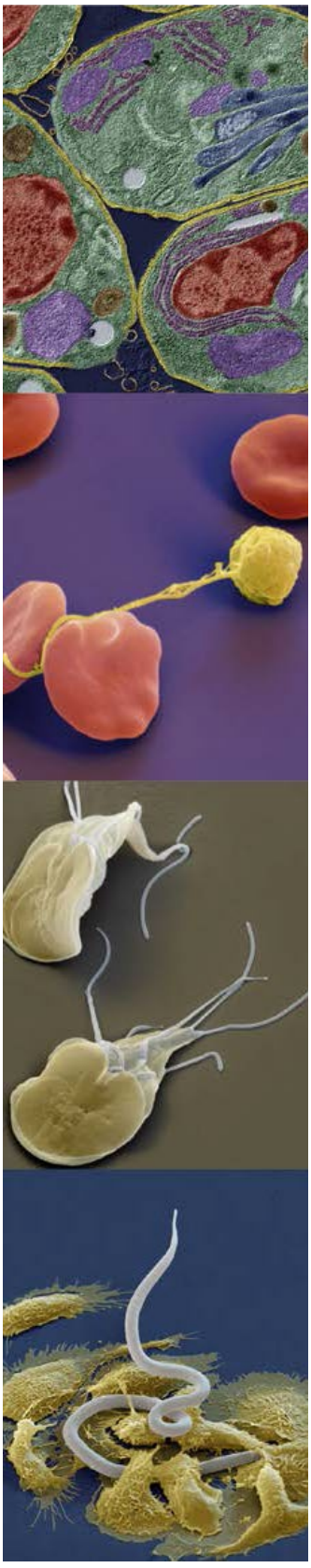
- Luis Elizalde (Project B4)

Scientific Writing

June 2, 2023 (ZIBI, Leonie Ringrose)

Taken from https//science-kitchen.net

As we are steadily approaching the ends of our PhDs, I thought it would be a good idea to improve on my writing skills. When joining the course, I realized that I actually never attended a formal writing course and had so far just relied on my intuition and feedback received over the years. Leonie Ringrose has a very active style of teaching, which is very refreshing and keeps you engaged at all times. She started giving this exact course as a PhD student herself but has refined it a lot over the years. This cumulated in a comprehensive writing book that covers all the major phrases used in the scientific style of writing. We didn't spend too much time talking about language however, but really focused on structure. We identified good and bad structure by taking apart papers that were picked by Leonie. In this manner, we worked through the major parts of a publication, namely the introduction, results, and discussion section. We talked about the main aims of each section and potential structure it can take before writing small paragraphs ourselves. I found it very refreshing to have a clearly defined structure



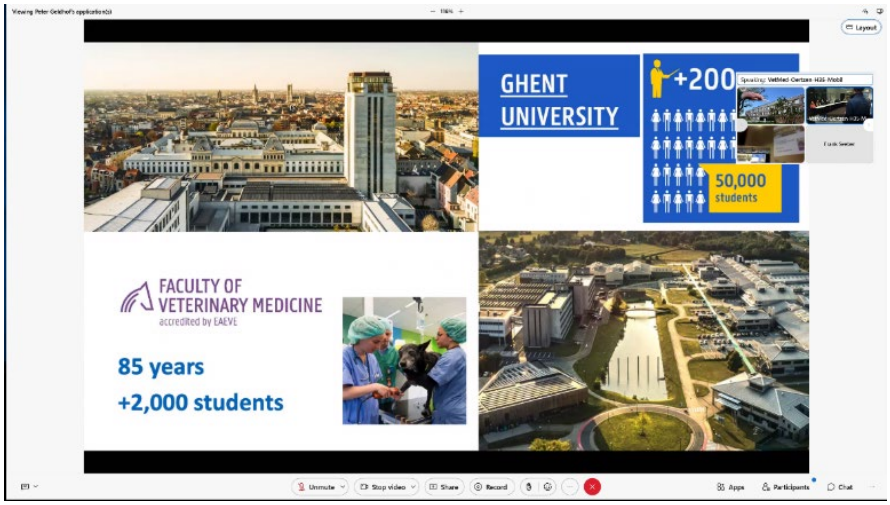
before writing, which certainly helps filling in the text and data later. The afternoons were also kept free so we could invest additional time in writing exercises that could be discussed with her to get some individual feedback.

I can really recommend this course to anyone not sure about how to best structure their publication. This shorter version of the course does not cover much language and might not be best suited for someone interested in improving their English. However, I think her insight into the exact meaning of common phrases helps to think twice when using them and were even interesting for native speakers.

- Otto Netzel (Project A6)

Berlin Parasitology Seminars (BPS)

Peter Geldhof
University of Ghent, December 13, 2022 (hybrid)



Screenshot by Marko Janke

In December last year, I had the opportunity to host Prof Peter Geldhof as our BPS guest. He is working at the department of Translational Physiology, Infectiology and Public Health at Ghent University in Belgium. There, he leads the laboratory for Parasitology and Parasitic Diseases where he is currently investigating four major lines of research: i) anti-nematode vaccine development with a focus on cattle parasites; ii) the use of serology to diagnose parasite infections in animals and humans with a strong focus on *Ascaris* and related nematode species; iii) the infection dynamics and development of immunity against *Giardia*;

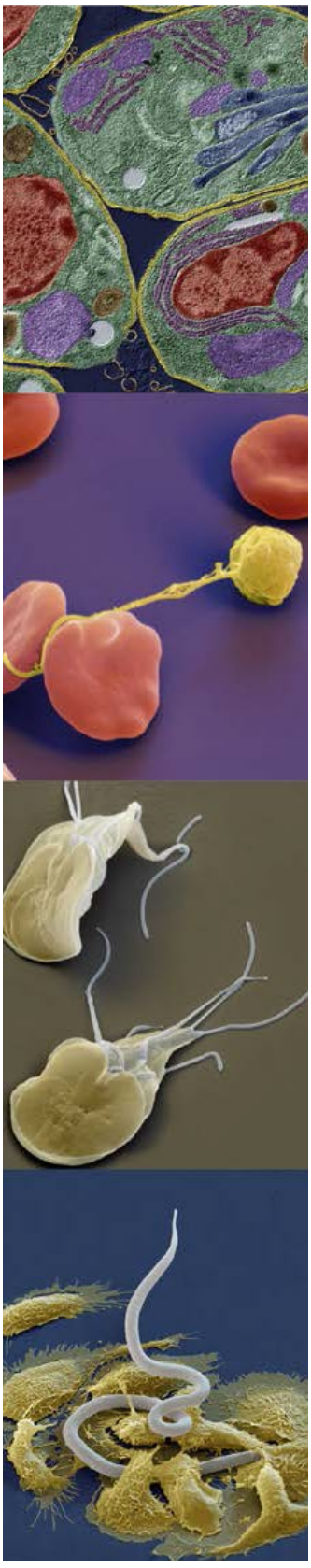


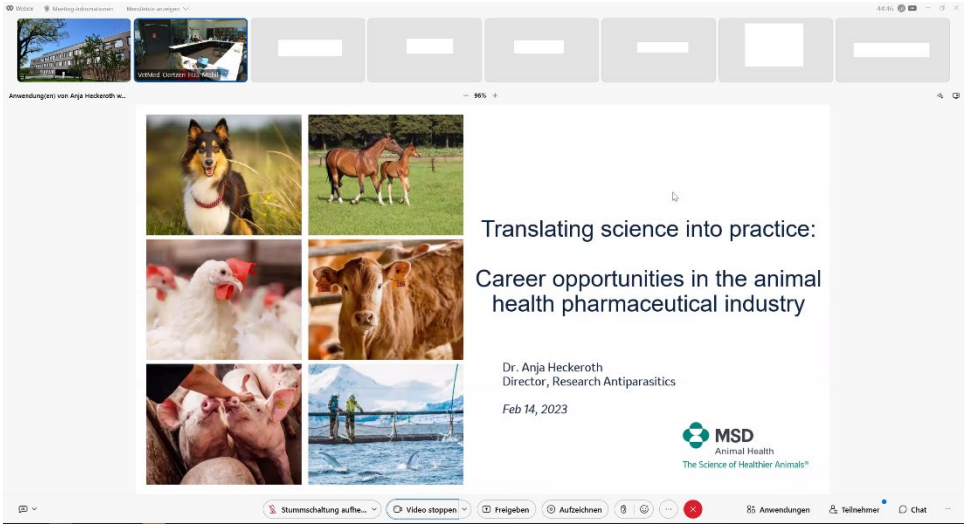
Photo by Marko Jankev

iv) the diagnosis, treatment, anthelmintic resistance of nematode infections in poultry. During his talk, Prof Geldhof gave us some insights into the first two aspect of his research. His talk with the title “Anti-nematode vaccine development and the use of serology to diagnose worm infections in animals and humans” was followed by a vivid discussion, and of course some delicious chocolate covered pretzels.

- Larissa Oser (Project C9)

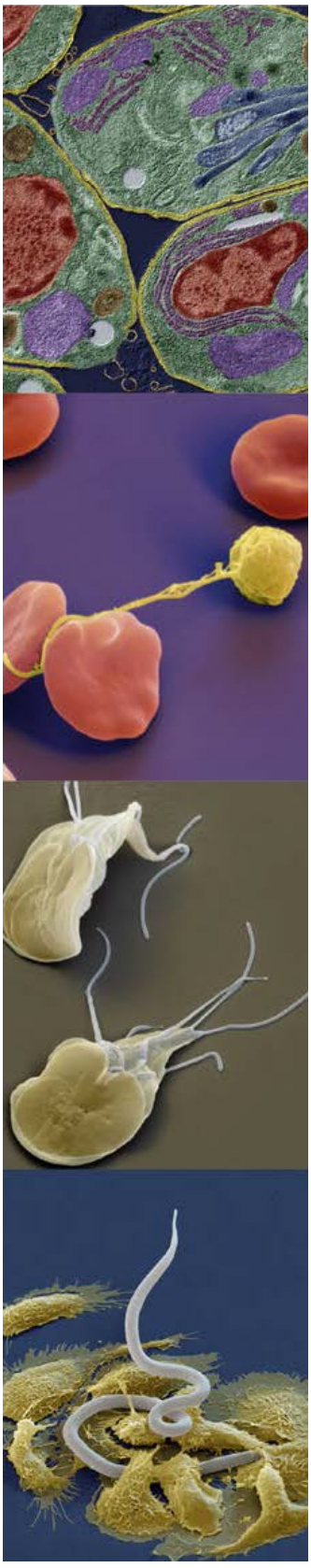
Anja Heckeroth

MSD, Munich, February 14, 2022 (hybrid)



Screenshot by Marko Janke

The first chapter of the new format BPS meets Career Options took place in February 2023. Here, guests from industry and other employers will introduce non-academical job options after completing a PhD thesis. This time, Anja Heckeroth from MSD Animal Health Innovation gave a talk entitled “Translating science into practice: Career opportunities in the animal health pharmaceutical industry” and shared a brief look in her job. MSD produces medicals, vaccines and biologicals for animal health. That may give different job options for graduated students, and not only for veterinarians. First, Anja Heckeroth introduced a new medical, which was developed in the MSD labs R&D to treat pet diseases. Then, she described some departments or sections in her company to visiualize different job profiles and options at MSD. This first



session of the new format can be considered as success. There is a call for career option seminars with our PhD students. Therefore, more career seminars are planned and will be performed at different events, like the PhD student symposium, the RTG Retreat or other formats.

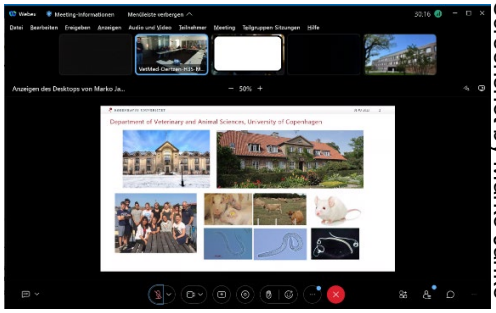
Photo by Marko Janke

- Marko

Andrew Williams
University of Copenhagen
March 1, 2023 (hybrid)

Photo by Marko Janke

In March this year, we welcomed Andrew Williams, PhD from the department of Veterinary and Animal Sciences at the university of Copenhagen in Berlin. He is an associate professor in the laboratory of Parasitology and Aquatic Pathobiology where he is currently investigating interactions between gut pathogens, immune function, the host diet and microbiota, both in mice and pigs. Moreover, he is studying novel antimicrobial compounds from natural plant sources and the parasite-induced modulation of inflammation and immunity. As usual, interested PhD students and PIs were given the opportunity to schedule a 1-to-1 meeting to discuss their own research with him, an offer that was well received by everybody. It was a great time for students and PI (both in person and online) to interact with him and discuss his interesting work, especially for all people working with large-animal models. After long meetings, Andrew gave us some insights into the previously mentioned aspects of his research. His talk was titled: “Diet, gut microbes and immunity to helminth infection”. We had a pleasant time discussing science and learning about the research performed in Andrew’s lab.



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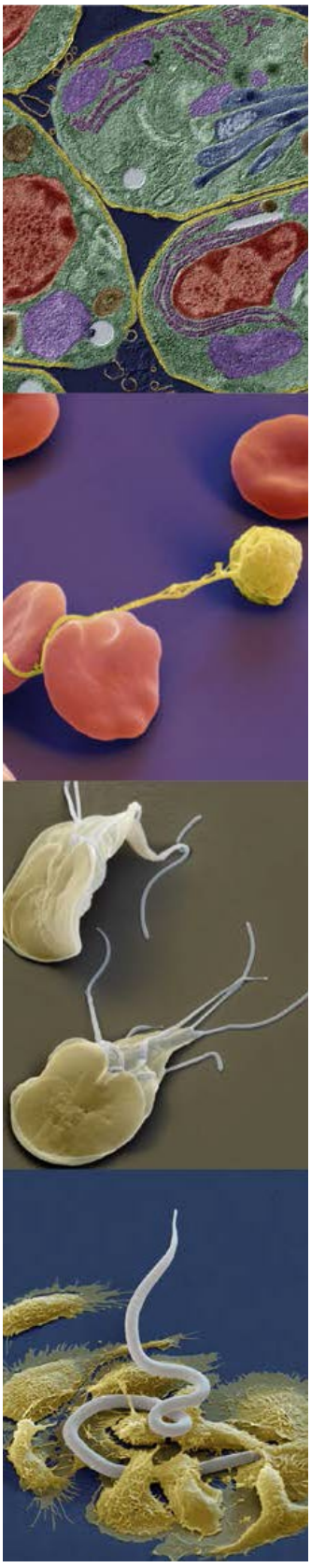
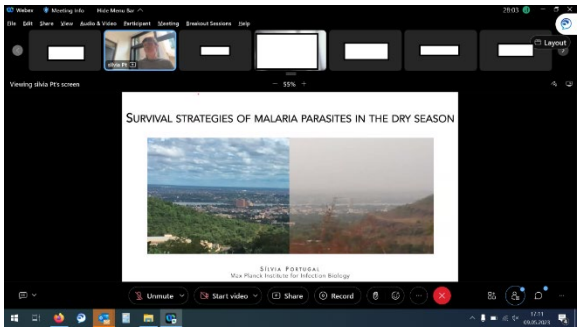
- Larissa Oser (Project C9)



Silvia Portugal
MPIIB
May 9, 2023 (hybrid)


Photo by Marko Janke

The *Plasmodium* malaria parasite relies on the *Anopheles* mosquito vector for its transmission to humans. However, in endemic regions like Mali, the dry season leads to the drying up of *Anopheles* mosquito breeding sites, resulting in a lack of mosquitoes. Dr Silvia Portugal's research group focuses on investigating the mechanisms utilized by the *Plasmodium* parasites to enter a dormant state within the human host during the dry season. This dormancy ensures their survival until the next wet season when transmission can resume. During her talk at the BPS, she shared some of the research that her group and her collaborating group from Kalifabougou in Mali are conducting to understand how parasites persist in the human host without causing symptoms or being detected.

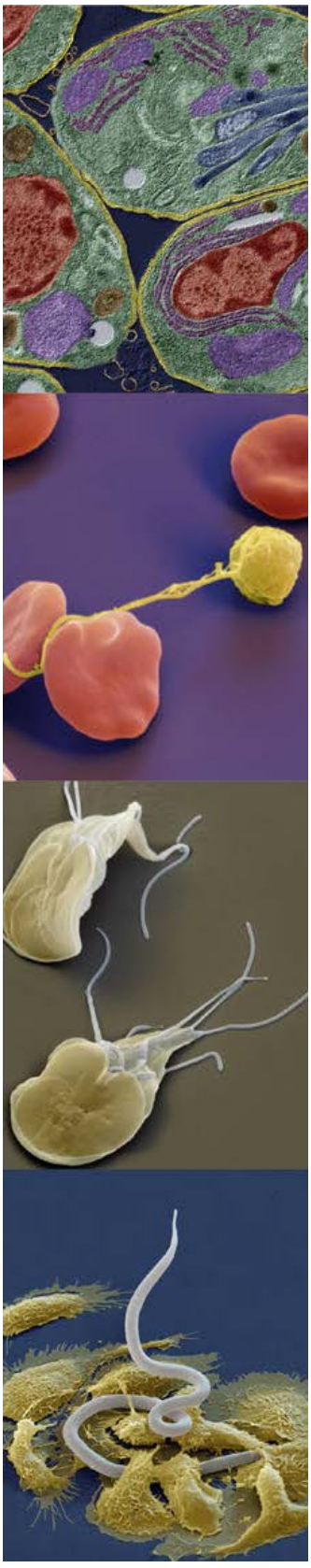


Screenshot by Marko Janke

A notable finding from the research conducted by Dr Silvia Portugal's group suggests that during the dry season, a significant proportion of *Plasmodium*-positive children exhibited considerably lower parasitaemia compare to clinical cases of malaria during the weat season. This phenomenon was attributed to the clearance of a large proportion of infected red blood cells by the spleen. This clearance mechanism allows the parasites to persist in the host while causing a diminished or non-immune response. The talk given by Dr Silvia Portugal was followed by an interesting discussion and finally by "pretzel and drinks."

Overall, the research presented by Silvia Portugal's group sheds light on the strategies employed by malaria parasites to survive and persist during the dry season in the absence of *Anopheles* mosquitoes. Understanding these mechanisms is crucial for developing effective interventions to control and eliminate malaria in endemic regions.

- Marly Erazo (Project C6)



Fieldwork

October 2022 – March 2023, Kenya

Between October 2022 and March 2023, I had an exciting experience in designing and conducting a study on *Ascaris* immune response characterization in about 400 school-going children from Western Kenya. I gained a wealth of experience in conducting human research and appreciating the value of humanity. I began with writing and defending my proposal for ethical approvals and acquiring relevant licenses. This was followed by informed consenting meetings, which were full of life due to the warm reception and knowledge expectancy from the teachers, parents, and children. Besides, I got an opportunity to teach the children about various worm infections and the need for maintaining hygiene to prevent infections. In addition, we donated the necessary materials for maintaining hygiene and treated the sick participants.
I managed to overcome several challenges and successfully performed a myriad of laboratory analysis including microscopy, flow cytometry, ELISA, PCR and microbiome sequencing among others.

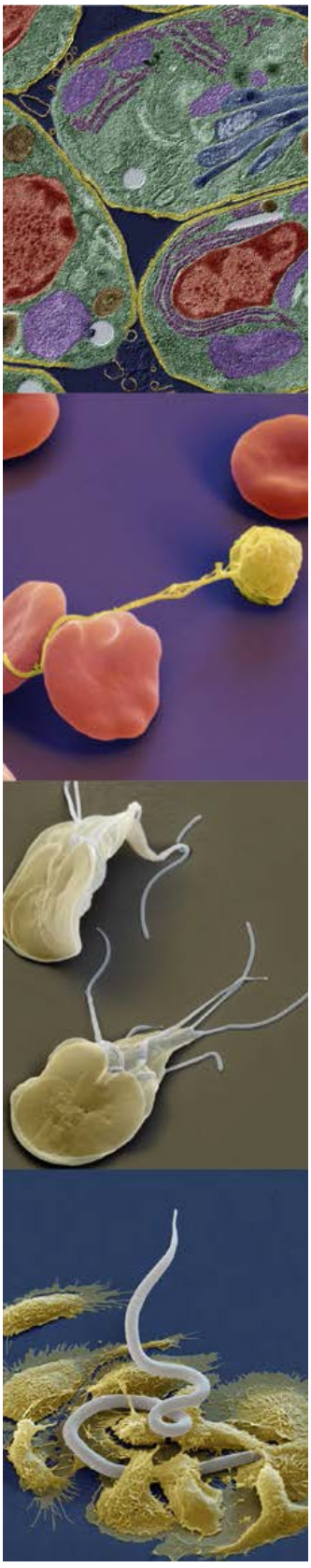
Photo by Robert Mugo: Pupils presenting a poem on the types of helminths, their effects and prevention measures.

- Robert Mugo (Project C9 associated)

Africa Workshop Fieldwork

March 20-31, 2023 (Namibia)

For most students, it was the first time going on a field trip in Africa, while for us, the Africans, it was our first time being in a Southern African country. It was really a long trip to Namibia, which left most of us stressed



up, but the warm reception from Dr Bettina Wachter and her team at the Hosea Kutako International airport invigorated us for the next two hours journey by car to the Okambara Elephant Lodge (which became our lab station as well as our residence). Upon arrival, we were allocated our various living spaces and we unpacked our luggages. In the evening, we converged and set up our field lab station. The lab was set up with 4 different working areas: DNA extraction, PCR and gel electrophoresis, Qubit and sequencing, “poop processing” and microscopy stations. We also had 6 different research teams working on different projects, which sometimes causes a bit of chaos in lab amidst the awesome and friendly teamwork environment. Most of the research teams start off very early in the morning to go and collect fecals, water or blood samples from wildlife or “wild farm” animals, water puddles and wild mice respectively. Upon return in the afternoon, the samples are processed for microscopy or DNA extraction and PCR. The different research groups then selected some samples, which were further combined for sequencing by the sequencing team led by Prof Emanuel Heitlinger.

Photo by Marko Janke: The Lab

The experiences were priceless; from optimizing PCR machines on the field (because field conditions differ from laboratory conditions in Berlin) to sticking of fingers into the butt of a warthog to collect fresh poop after it had been shot by hunters. We did not shot animals exclusively for scientific reasons, but analyzed animals, which were shot by hunters anyway or found dead. It was also exciting see PIs and students stay in the lab late at night still processing and analyzing samples. It was usally hectic times in the lab, however we all had our turns to embark on game drives to have close interactions with wildlife, observe cheetahs being fed or go for a “stroll in the jungle” to cool off our heads. We will not forget the gastronomy lectures we got at every supper time with the wonderful chefs at the Okambara Lodge. Goodbyes are always sad times, nonetheless, we had to leave the lodge to another farm (the farm of the Litchenberg family) to prepare for departure. It was a great experience touring big farms on the back of pick-up trucks, receiving botany and zoology lectures from the Lictenbergs, being beaten by rain and seeing wild

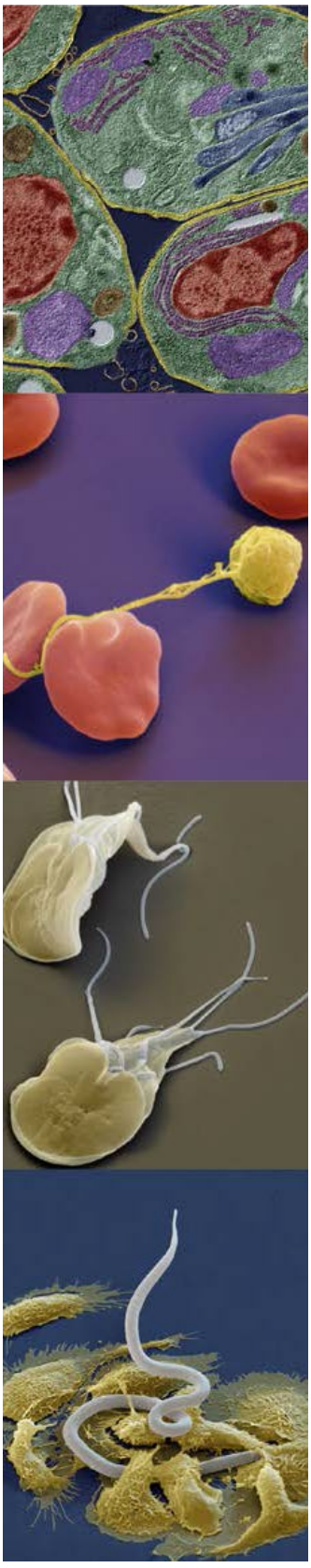


Photo by Marko Janke: Outdoor lectures

animals in their natural habitat interact with the ecosystem. I also personally enjoyed the cheetah research lecture by Dr Bettina Wachter, which in my opinion was very inspiring.

Overall, Namibia was a great learning and field experience, which will go a long way to enhance our perspective of science and research in the context of field work. We will want to use this medium to thank all the funders, organizers, PIs, especially Dr Bettina Wachter and her team for making this possible.
- Joshua Adjah (Project B5)

Upcoming Events

Berlin Parasitology Seminars

September 26, 2023, 5pm – **Lisa Reynolds** (University of Victoria, Victoria BC, Canada, remote), *Helminth infection-induced changes in intestinal metabolites and the consequences for intestinal immunity*

October 10, 2023, 5pm – **Marc Nicolas Faber** (Moredun Research Institute, Midlothian, Scotland, hybrid), *Disruptive technologies in veterinary GI-nematodes: From 3D organoid culture to spatial transcriptomics*

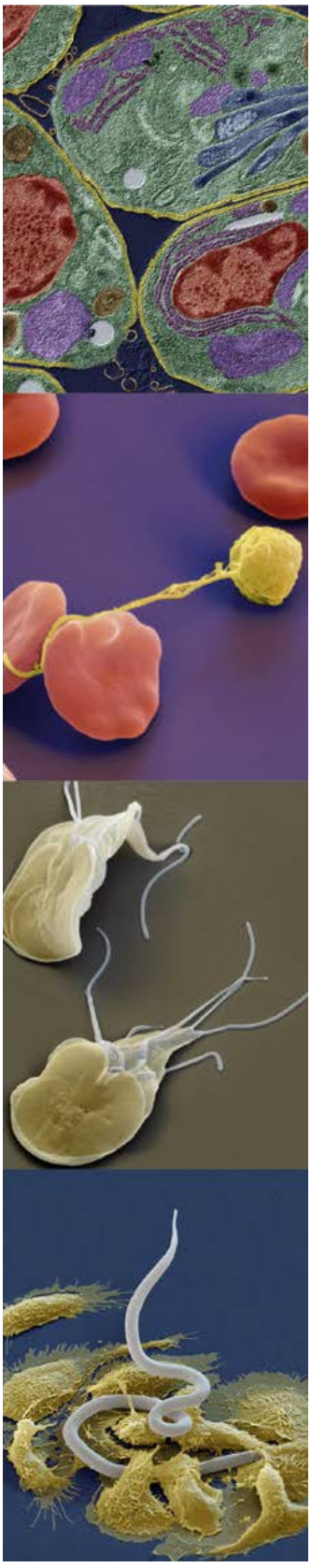
December 12, 2023, 5pm – **Joseph Turner** (Liverpool School of Tropical Medicine, Liverpool, UK, remote), *tba*

Other events

August 7-9, 2023 – PhD student symposium (Hotel Villago, Eggersdorf bei Strausberg)

October 24-25, 2023 – GRK 2046 Retreat (VP, Düppel)

November 21, 2023 – ZIBI Students' Day by GRK 2046



Graduated GRK 2046 students

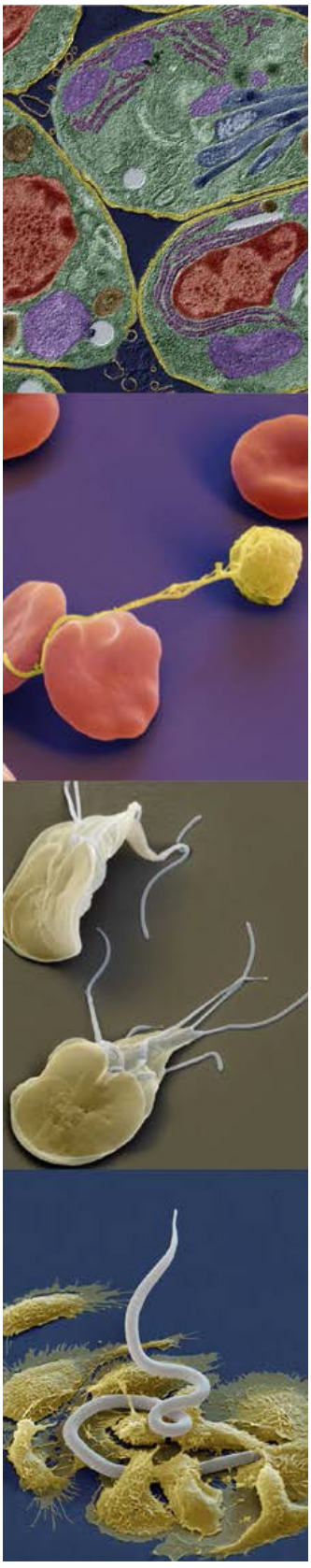
Congratulations to our second generation PhD student Robin Benter (project C6, date of defense: 27.01.2023).

Publications

Smaller size packs a stronger punch - Recent advances in small antibody fragments targeting tumour-associated carbohydrate antigens.

Khilji SK, Op 't Hoog C, **Warschkau D**, **Lühle J**, **Goerdeler** F, Freitag A, **Seeberger PH**, **Moscovitz O**. (2023).
Theranostics 13:3041-3063. doi: 10.7150/thno.80901.

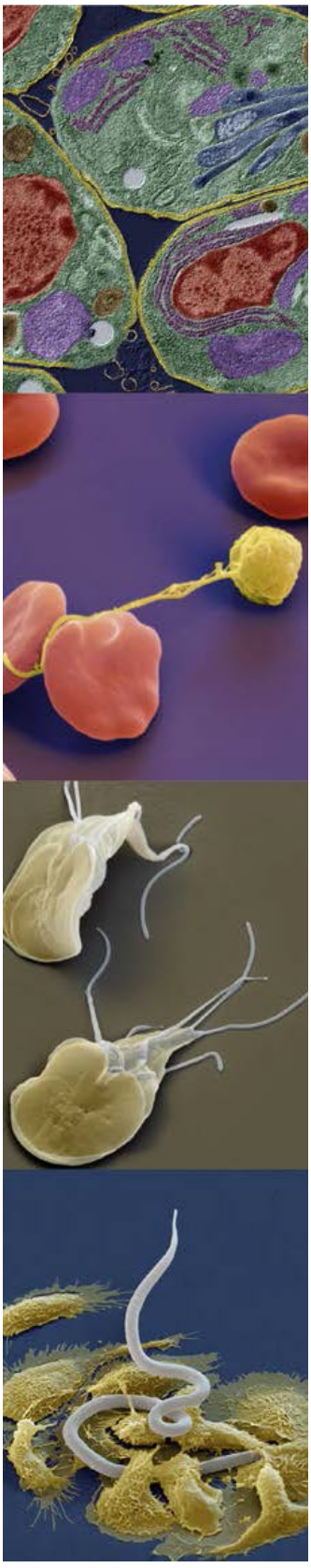
Abstract:
Attached to proteins, lipids, or forming long, complex chains, glycans represent the most versatile post-translational modification in nature and surround all human cells. Unique glycan structures are monitored by the immune system and differentiate self from non-self and healthy from malignant cells. Aberrant glycosylations, termed tumour-associated carbohydrate antigens (TACAs), are a hallmark of cancer and are correlated with all aspects of cancer biology. Therefore, TACAs represent attractive targets for monoclonal antibodies for cancer diagnosis and therapy. However, due to the thick and dense glycocalyx as well as the tumour micro-environment, conventional antibodies often suffer from restricted access and limited effectiveness *in vivo*. To overcome this issue, many small antibody fragments have come forth, showing similar affinity with better efficiency than their full-length counterparts. Here we review small antibody fragments against specific glycans on tumour cells and highlight their advantages over conventional antibodies.



Amplicon sequencing allows differential quantification of closely related parasite species: an example from rodent Coccidia (*Eimeria*).

Ferreira SCM, **Jarquín-Díaz VH**, **Heitlinger E**. (2023).
Parasit Vectors 16:204. doi: 10.1186/s13071-023-05800-6.

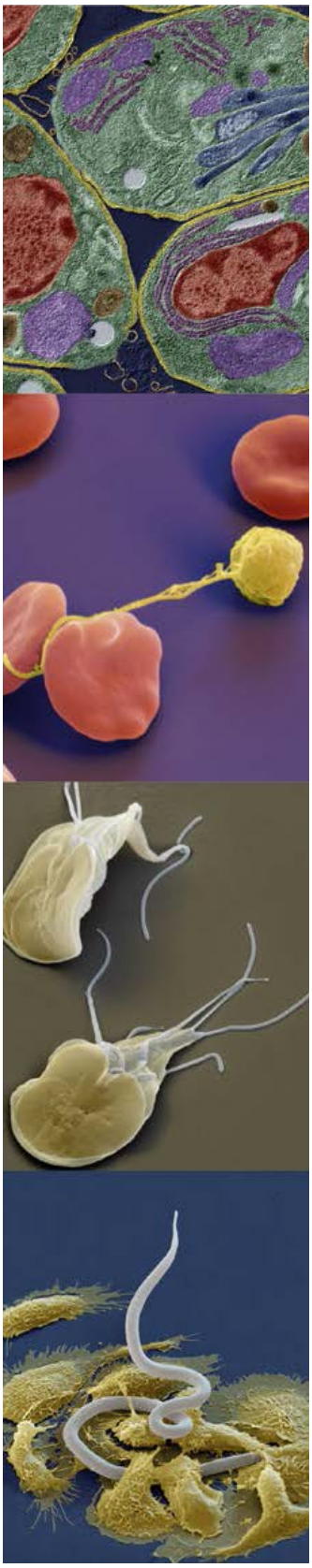
Abstract:
Background Quantifying infection intensity is a common goal in parasitological studies. We have previously shown that the amount of parasite DNA in faecal samples can be a biologically meaningful measure of infection intensity, even if it does not agree well with complementary counts of transmission stages (oocysts in the case of Coccidia). Parasite DNA can be quantified at relatively high throughput using quantitative polymerase chain reaction (qPCR), but amplification needs a high specificity and does not simultaneously distinguish between parasite species. Counting of amplified sequence variants (ASVs) from high-throughput marker gene sequencing using a relatively universal primer pair has the potential to distinguish between closely related co-infecting taxa and to uncover the community diversity, thus being both more specific and more open-ended.
Methods We here compare qPCR to the sequencing-based amplification using standard PCR and a microfluidicsbased PCR to quantify the unicellular parasite *Eimeria* in experimentally infected mice. We use multiple amplicons to differentially quantify *Eimeria* spp. in a natural house mouse population.
Results We show that sequencing-based quantification has high accuracy. Using a combination of phylogenetic analysis and the co-occurrence network, we distinguish three *Eimeria* species in naturally infected mice based on multiple marker regions and genes. We investigate geographical and host-related effects on *Eimeria* spp. Community composition and find, as expected, prevalence to be largely explained by sampling locality (farm). Controlling for this effect, the novel approach allowed us to find body condition of mice to be negatively associated with *Eimeria* spp. abundance.
Conclusions We conclude that amplicon sequencing provides the underused potential for species distinction and simultaneous quantification of parasites in faecal material. The method allowed us to detect a negative effect of *Eimeria* infection on the body condition of mice in the natural environment.



Infection with soil-transmitted helminths and their impact on coinfections.

Schlosser-Brandenburg J, Midha A, **Mugo RM**, Ndombi EM, Gachara G, Njomo D, **Rausch S**, **Hartmann S**. (2023).
Front Parasitol published May 24. doi: 10.3389/fpara.2023.1197956.

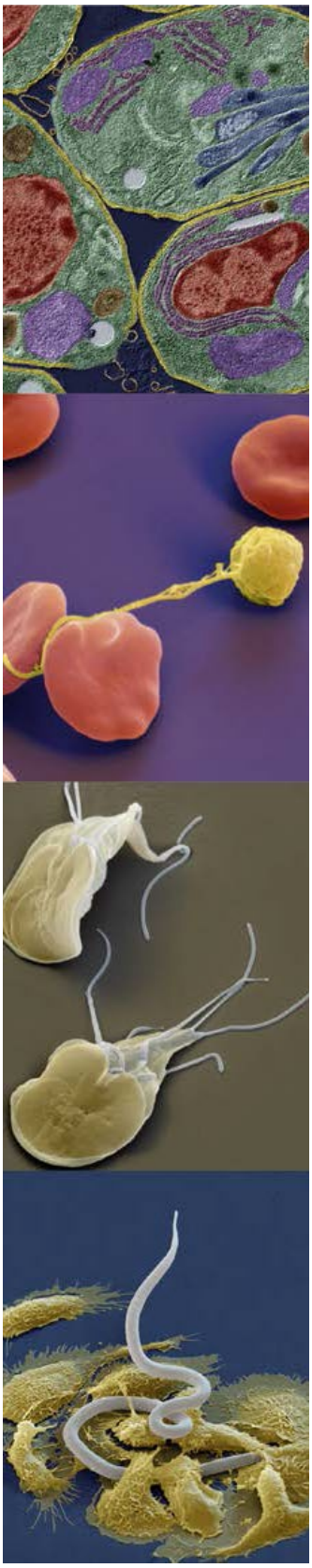
Abstract:
The most important soil-transmitted helminths (STHs) affecting humans are roundworms, whipworms, and hookworms, with a large proportion of the world's population infected with one or more of these intestinal parasites. On top of that, concurrent infections with several viruses, bacteria, protozoa, and other helminths such as trematodes are common in STH-endemic areas. STHs are potent immunomodulators, but knowledge about the effects of STH infection on the direction and extent of coinfections with other pathogens and *vice versa* is incomplete. By focusing on Kenya, a country where STH infections in humans are widespread, we provide an exemplary overview of the current prevalence of STH and co-occurring infections (e.g. with Human Immunodeficiency Virus, *Plasmodium falciparum*, *Giardia duodenalis* and *Schistosoma mansoni*). Using human data and complemented by experimental studies, we outline the immunomechanistic interactions of coinfections in both acutely STH transmigrated and chronically infected tissues, also highlighting their systemic nature. Depending on the coinfecting pathogen and immunological readout, STH infection may restrain, support, or even override the immune response to another pathogen. Furthermore, the timing of the particular infection and host susceptibility are decisive for the immunopathological consequences. Some examples demonstrated positive outcomes of STH coinfections, where the systemic effects of these helminths mitigate the damage caused by other pathogens. Nevertheless, the data available to date are rather unbalanced, as only a few studies have considered the effects of coinfection on the worm's life cycle and associated host immunity. These interactions are complex and depend largely on the context and biology of the coinfection, which can act in either direction, both to the benefit and detriment of the infected host.



Highly contiguous genomes of human clinical isolates of *Giardia duodenalis* reveal assemblage- and sub-assemblage-specific presence-absence variation in protein-coding genes.

Klotz C, Schmid MW, Winter K, Ignatius R, Weisz F, Saghaug CS, Langeland N, Dawson S, Lalle M, Hanevik K, Cacciò SM, **Aebischer T**. (2023). ***Microb Genom*** 9:mgen000963. doi: 10.1099/mgen.0.000963.

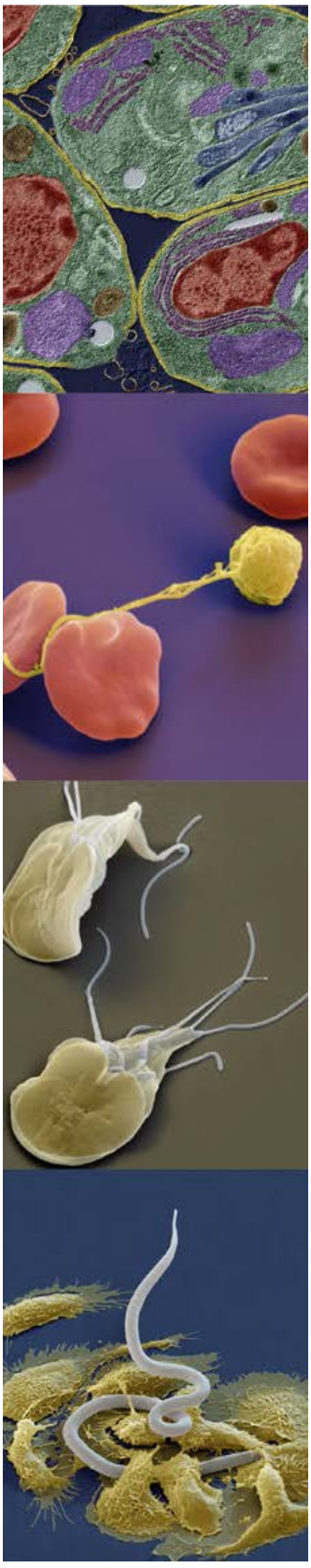
Abstract:
Giardia duodenalis (syn. *G. intestinalis*, *G. lamblia*) is a widespread gastrointestinal protozoan parasite with debated taxonomic status. Currently, eight distinct genetic sub-groups, termed assemblages A-H, are defined based on a few genetic markers. Assemblages A and B may represent distinct species and are both of human public health relevance. Genomic studies are scarce and the few reference genomes available, in particular for assemblage B, are insufficient for adequate comparative genomics. Here, by combining long- and short-read sequences generated by PacBio and Illumina sequencing technologies, we provide nine annotated genome sequences for reference from new clinical isolates (four assemblage A and five assemblage B parasite isolates). Isolates chosen represent the currently accepted classification of sub-assemblages AI, AII, BIII and BIV. Synteny over the whole genome was generally high, but we report chromosome-level translocations as a feature that distinguishes assemblage A from B parasites. Orthologue gene group analysis was used to define gene content differences between assemblage A and B and to contribute a gene-set-based operational definition of respective taxonomic units. *Giardia* is tetraploid, and high allelic sequence heterogeneity (ASH) for assemblage B vs. assemblage A has been observed so far. Noteworthy, here we report an extremely low ASH (0.002%) for one of the assemblage B isolates (a value even lower than the reference assemblage A isolate WB-C6). This challenges the view of low ASH being a notable feature that distinguishes assemblage A from B parasites, and low ASH allowed assembly of the most contiguous assemblage B genome currently available for reference. In conclusion, the description of nine highly contiguous genome assemblies of new isolates of *G. duodenalis* assemblage A and B adds to our understanding of the genomics and species population structure of this widespread zoonotic parasite.



Immunization with excretory-secretory molecules of intestinal nematodes induces antigen-specific protective memory Th2 cell responses.

Yordanova IA, **Elizalde-Velázquez LE**, **Hartmann S**. (2023).
Eur J Immunol Feb 13:e2250237. doi: 10.1002/eji.202250237.

Abstract:
Parasitic nematodes infect more than 1 billion people in the global south. The development of effective antihelminthic vaccines is a crucial tool for their future elimination. Protective immune responses to nematodes depend on Gata3+ Th2 cells, which can also be induced by nematode-released products. Whether these nematode products induce antigen-specific long-lived memory T cells and thereby confer protection against a challenge infection is not known yet. Hence, we set out to characterize the formation of memory Th2 cells induced by immunization with *Heligmosomoides polygyrus* excretory-secretory (HES) products, infection-induced versus immunization-induced recall responses to a challenge infection, and whether HES-induced memory T cells show protective properties following adoptive transfer. Our results show that 8 weeks postimmunization, HES induces long-lived functional memory Th2 cells at the site of immunization in the peritoneal cavity. Following a *H. polygyrus* challenge infection, HES-immunized mice display MHC-II-dependent antigen-specific Th2 cytokine responses in the gut-draining lymph nodes, comparable to those induced by a prior natural infection. Moreover, adoptive transfer of sorted memory CD4+ T cells from HES-immunized donors reduces female worm fecundity following a challenge *H. polygyrus* infection in recipient mice, highlighting a protective role for immunization-induced memory T cells.



Significant, but not biologically relevant: *Nosema ceranae* infections and winter losses of honey bee colonies.

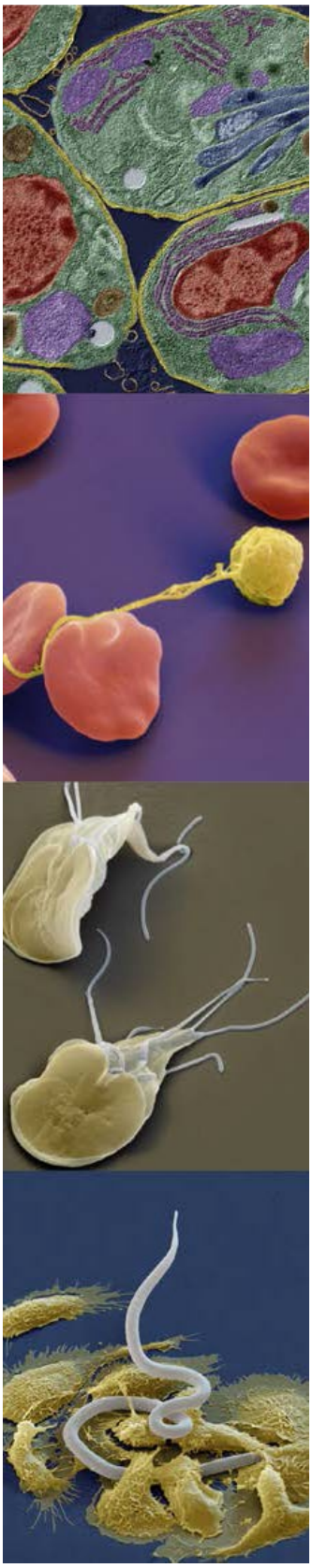
Schüler V, Liu YC, Gisder S, Horchler L, Groth D, **Genersch E**. (2023).
Commun Biol *6:229. doi: 10.1038/s42003-023-04587-7*.

Abstract:
The Western honey bee *Apis mellifera*, which provides about 90% of commercial pollination, is under threat from diverse abiotic and biotic factors. The ectoparasitic mite *Varroa destructor* vectoring deformed wing virus (DWV) has been identified as the main biotic contributor to honey bee colony losses worldwide, while the role of the microsporidium *Nosema ceranae* is still controversially discussed. In an attempt to solve this controversy, we statistically analyzed a unique data set on honey bee colony health collected from a cohort of honey bee colonies over 15 years and comprising more than 3000 data sets on mite infestation levels, *Nosema* spp. infections, and winter losses. Multivariate statistical analysis confirms that *V. destructor* is the major cause of colony winter losses. Although *N. ceranae* infections are also statistically significantly correlated with colony losses, determination of the effect size reveals that *N. ceranae* infections are of no or low biological relevance.

Advances towards the complete *in vitro* life cycle of *Toxoplasma gondii*.

Warschkau D, **Seeber F**. (2023).
Fac Rev 12:1. doi: 10.12703/r/12-1

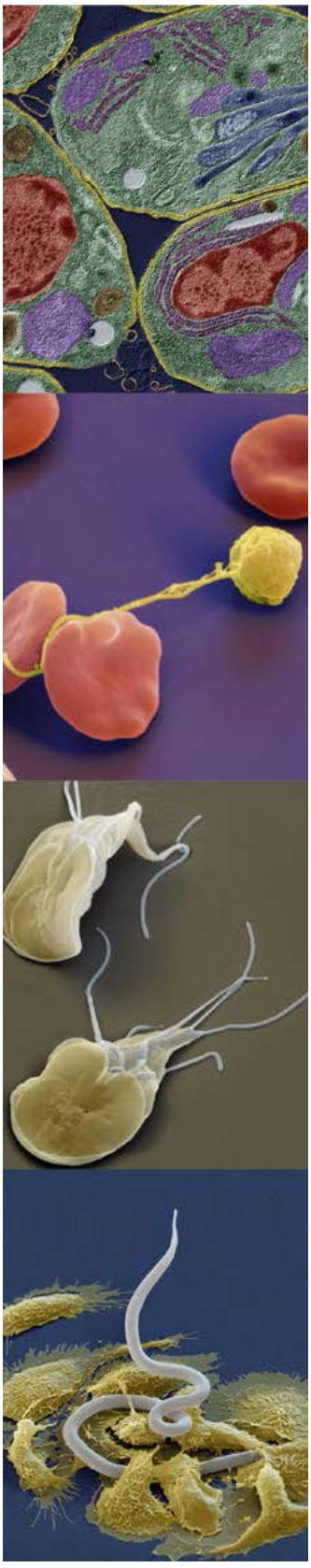
Abstract:
The full life cycle of *Toxoplasma gondii* cannot be recapitulated *in vitro*, and access to certain stages, such as mature tissue cysts (bradyzoites) and oocysts (sporozoites), traditionally requires animal experiments. This has greatly hindered the study of the biology of these morphologically and metabolically distinct stages, which are essential for the infection of humans and animals. However, several breakthrough advances have been made in recent years towards obtaining these life stages *in vitro*, such as the discovery of several molecular factors that induce differentiation and commitment to the sexual cycle, and different culture methods that use, for example, myotubes and intestinal organoids to obtain mature bradyzoites and different sexual stages of the parasite. We review these novel tools and approaches, highlight their limitations and challenges, and discuss what research questions can already be answered with these models. We finally identify future routes for recapitulating the entire sexual cycle *in vitro*.



Late Embryogenesis Abundant Proteins Contribute to the Resistance of *Toxoplasma gondii* Oocysts against Environmental Stresses.

Arranz-Solís D*, **Warschkau D*, Fabian BT**, **Seeber F**, Saeij JPJ. (2023). ***mBio*** Feb 21:e0286822. doi: 10.1128/mbio.02868-22. *equal contribution.

Abstract:
Toxoplasma gondii oocysts, which are shed in large quantities in the feces from infected felines, are very stable in the environment, resistant to most inactivation procedures, and highly infectious. The oocyst wall provides an important physical barrier for sporozoites contained inside oocysts, protecting them from many chemical and physical stressors, including most inactivation procedures. Furthermore, sporozoites can withstand large temperature changes, even freeze-thawing, as well as desiccation, high salinity, and other environmental insults; however, the genetic basis for this environmental resistance is unknown. Here, we show that a cluster of four genes encoding Late Embryogenesis Abundant (LEA)-related proteins are required to provide *Toxoplasma* sporozoites resistance to environmental stresses. *Toxoplasma* LEA-like genes (TgLEAs) exhibit the characteristic features of intrinsically disordered proteins, explaining some of their properties. Our *in vitro* biochemical experiments using recombinant TgLEA proteins show that they have cryoprotective effects on the oocyst-resident lactate dehydrogenase enzyme and that induced expression in *E. coli* of two of them leads to better survival after cold stress. Oocysts from a strain in which the four LEA genes were knocked out en bloc were significantly more susceptible to high salinity, freezing, and desiccation compared to wild-type oocysts. We discuss the evolutionary acquisition of LEA-like genes in *Toxoplasma* and other oocyst-producing apicomplexan parasites of the *Sarcocystidae* family and discuss how this has likely contributed to the ability of sporozoites within oocysts to survive outside the host for extended periods. Collectively, our data provide a first molecular detailed view on a mechanism that contributes to the remarkable resilience of oocysts against environmental stresses. **IMPORTANCE** *Toxoplasma gondii oocysts* are highly infectious and may survive in the environment for years. Their resistance against disinfectants and irradiation has been attributed to the oocyst and sporocyst walls by acting as physical and permeability barriers. However, the genetic basis for their resistance against stressors like changes in temperature, salinity, or humidity, is unknown. We show that a cluster of four genes encoding *Toxoplasma* Late Embryogenesis Abundant (TgLEA)-related proteins are important for this resistance to environmental stresses. TgLEAs have features of intrinsically disordered proteins, explaining some of their properties. Recombinant TgLEA proteins show cryoprotective effects on the parasite's lactate dehydrogenase, an abundant enzyme in oocysts, and expression in *E. coli* of two TgLEAs has a beneficial effect on growth after cold stress. Moreover, oocysts from a strain lacking all four TgLEA genes were more susceptible to high salinity, freezing, and desiccation compared to wild-type oocysts, highlighting the importance of the four TgLEAs for oocyst resilience.



Changes in the *Ixodes ricinus* microbiome associated with artificial tick feeding.

Militzer N, Pinecki Socias S, Nijhof AM. (2023).
Front Microbiol 13:1050063. doi: 10.3389/fmicb.2022.1050063.

Abstract:
Artificial tick feeding systems (ATFS) can be used to study tick biology and tick-pathogen interactions. Due to the long feeding duration of hard ticks, antibiotics are commonly added to the *in vitro* blood meal to prevent the blood from decaying. This may affect the ticks' microbiome, including mutualistic bacteria that play an important role in tick biology. This effect was examined by the consecutive feeding of *Ixodes ricinus* larvae, nymphs, and adults *in vitro* with and without the supplementation of gentamicin and in parallel on calves. DNA extracted from unfed females was analyzed by 16S rRNA sequencing. The abundance of *Candidatus Midichloria mitochondrii*, *Rickettsia helvetica* and *Spiroplasma* spp. was measured by qPCR in unfed larvae, nymphs, and adults. Larvae and nymphs fed on calves performed significantly better compared to both *in vitro* groups. Adults fed on blood supplemented with gentamicin and B vitamins had a higher detachment proportion and weight compared to the group fed with B vitamins but without gentamicin. The detachment proportion and weights of females did not differ significantly between ticks fed on calves and *in vitro* with gentamicin, but the fecundity was significantly higher in ticks fed on calves. 16S rRNA sequencing showed a higher microbiome species richness in ticks fed on calves compared to ticks fed in vitro. A shift in microbiome composition, with Ca. Midichloria mitochondrii as dominant species in females fed as juveniles on calves and R. helvetica as the most abundant species in females previously fed in vitro was observed. Females fed in vitro without gentamicin showed significant lower loads of Ca. M. mitochondrii compared to females fed in vitro with gentamicin and ticks fed on calves. Spiroplasma spp. were exclusively detected in female ticks fed on cattle by qPCR, but 16S rRNA sequencing results also showed a low abundance in in vitro females exposed to gentamicin. In conclusion, the employed feeding method and gentamicin supplementation affected the ticks' microbiome composition and fecundity. Since these changes may have an impact on tick biology and vector competence, they should be taken into account in studies employing ATFS.

Happy summer break!

Happy summer break!

- Marko