

# GRK 2046 Newsletter December 2020

## Summary, Update and News

Please enjoy the 10<sup>th</sup> edition of our biannual GRK 2046 newsletter. As usual, we report from workshops, seminars / lectures, publications and more.

**The bad news:** Due to the coronavirus situation, work-related travel to conferences etc. is still restricted. Social contacts (e.g. at our retreat or seminars) were completely abolished and also remain restricted.

**The good news:** We successfully relaunched our BPS / Role Models series, now ONLINE. The online sessions are going well. So, we were not happy but grateful to switch our annual retreat as well as the assessment center for recruiting the third PhD student generation to ONLINE mode. More information and photos (aka screenshots) in this edition.

We strongly believe that this virus called SARS-CoV-2 will continuously damp our researcher life for the next month or longer and eagerly await a vaccination.

Meanwhile, stay safe, stay healthy!

– Marko

## Conferences & Workshops

### Projektmanagement in der Forschung- traditionell, agil, hybrid

March 2020, Berlin

We were one of the last lucky people who still had time attending a real-

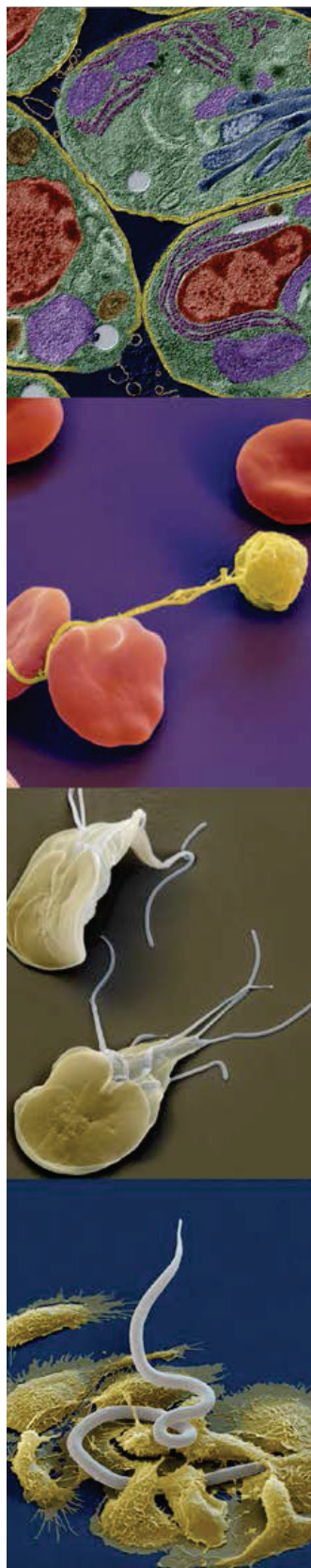


life workshop before the first corona lockdown 2020 was about to set up. Here, we participated in the project management

course “Projektmanagement in der Forschung- traditionell, agil, hybrid” at Freie Universität by Sven Aden, the founder and CEO of Aden Training, Advertisement and Moderation. In total, we were 13 participants at different academic career stages (doctorate

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candidates, post-docs, guest professors, or academic consultation staff) and different thematic backgrounds from social sciences (art history, ethology, educational science), but also from life sciences (biology, veterinary medicine, psychology, computer science). Furthermore, some participants already had run BMBF or DFG projects, were about to start projects or were explicitly set in a project management position to coordinate and manage.



During this two-day intensive course, we were introduced to different methods of project management especially considering traditional tools such as mile stones or agile project management tools (which originate from IT sector) with a focus on SCRUM. Here, we were able to go through each step from project planning, SMART principles, analyses of stake holders, risk management, to final reports and many more. Therefore, we had theoretical parts, but most interestingly we also worked on real-life project examples and experiments, train and brain stormed many tools of project management. To sum up, this course is informative and participatory and we would highly recommend this class to whoever is interested in improving and practicing their project management skills.

– Nina Militzer and Sophia Pinecki



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### **29th Annual Meeting of the German Society for Parasitology**

March 2020, Bonn → March 2021 (online)

Almost all of us had planned to attend this year's meeting of the German Society for Parasitology. We had sent our abstracts and the GRK2046 was even organizing a workshop as part of the conference. Unfortunately, the event was cancelled at the last minute and postponed to next year where it is going to take place online instead.

We are now looking forward to the online conference in 2021!

– Felix Goerdeler

### **Good X Practice**

7<sup>th</sup>-11<sup>th</sup> September (online)

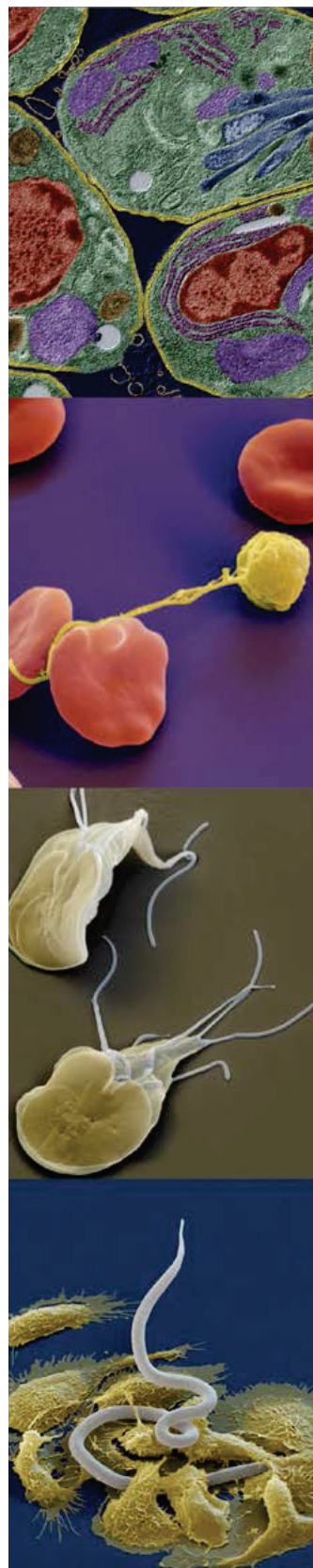
The btS organized a GxP intensive training course offered by the Pharmaakademie which took place during one week in September. GxP describes a general term for the guidelines of good working practice. These comprises the manufacturing of drugs, laboratory *in vitro* testing of these drugs in e.g. cell culture to identify potential hazards for humans and the environment, clinical practice to conduct clinical studies and the pharmacovigilance of drugs that were admitted to the market. The course offered a less intense study of laws regarding drug manufacturing and admission. It focused more on general aspects of good laboratory practice and how projects, with a priority on clinical studies, are managed in industry to ensure the safety at every single step of drug testing. Besides, the course allowed to think of future job opportunities not only in industry but also at governmental institutes, e.g. for drug administration. Finally, the course concluded with an online multiple-choice examination. We would like to thank the GRK for giving us the opportunity to participate.

– Irina Diekmann and Natalie Jakobs

### **Annual GRK retreat**

29<sup>th</sup>-30<sup>th</sup> October 2020 (online)

For the first time, the GRK retreat was held online this year. It was really nice to see everyone again after such a long time of corona-caused break and the organizing committee (thanks, Bhavya, David, Estefanía and Robin!) did a fantastic job. Although it was definitely a challenge to give

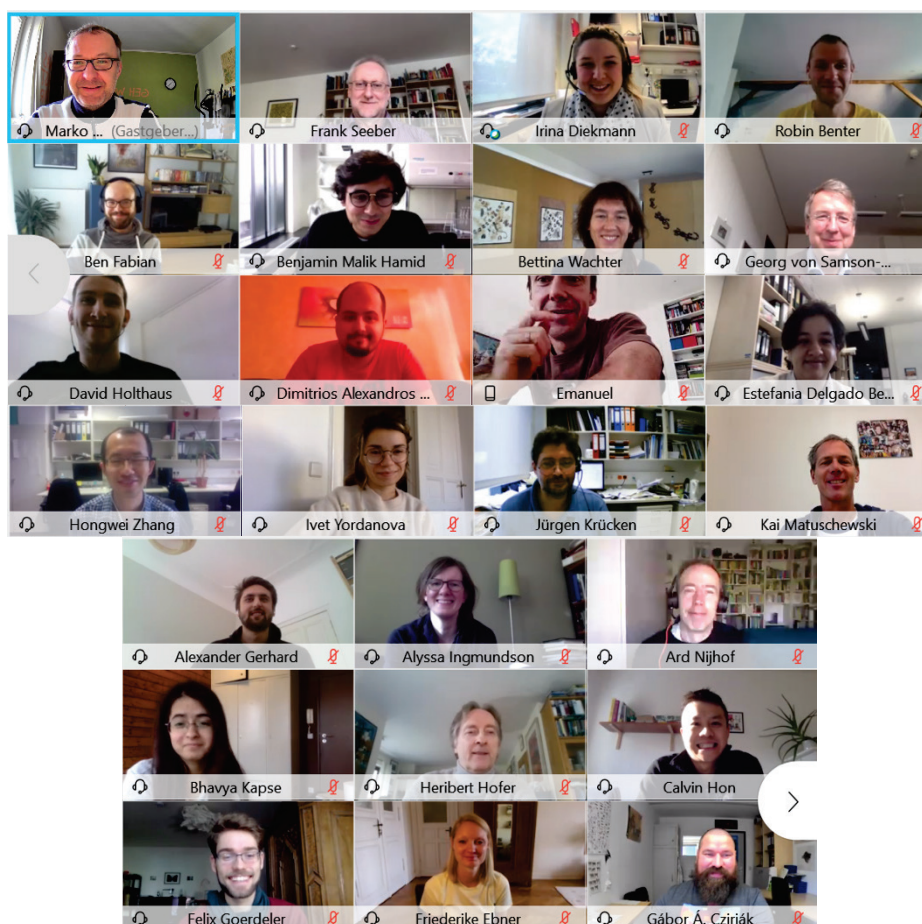


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a talk without being able to make eye contact, in my opinion everybody did great!

On the first day, we enjoyed talks from all PhD students of the GRK in four different sessions (nematode infections, wildlife parasitology, vectors/vector-borne diseases, protozoan parasites) and the discussions after the talks were really fruitful.

On the second day, three GRK alumnae joined us for the alumni\*ae session where we could learn from their experiences after the PhD and ask all our questions regarding their career paths.



Despite the online format of the retreat, we even managed to take a group photo and if we are lucky, maybe next year we can meet in person again!

– Felix Goerdeler



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### Antibody Engineering & Therapeutics Conference

14<sup>th</sup>-16<sup>th</sup> December (online)

The AET conference, organized by The Antibody Society, also had to take place online this year. Nonetheless, I was quite excited to join as this was my first time giving a talk at a conference. Fortunately, the virtual platform was very well structured and gave also the time and space to interact with other attendees.

Since almost all talks were available on-demand prior to the conference, I could choose talks based on my research interests and listen to them at my own speed – this was really helpful for us Europeans who were six hours ahead of Eastern time. Talks covered all areas of antibody research from antibody-drug conjugations and bispecific antibodies to antibody fragments and novel antibody-based therapies and were very informative.

The talks were alternated with live panel discussions, keynote presentations and poster sessions giving everyone the chance to ask questions that came up during the talks. During the breaks, there was even the possibility to meet and network with other attendees in virtual rooms. I believe everyone (including myself) was really grateful for the opportunity to present their ideas and to connect with people since networking has become so difficult this year.

All in all, I enjoyed the virtual edition of the AET conference very much and I can only recommend to give (other) virtual conferences a try for the remaining time of the pandemic.

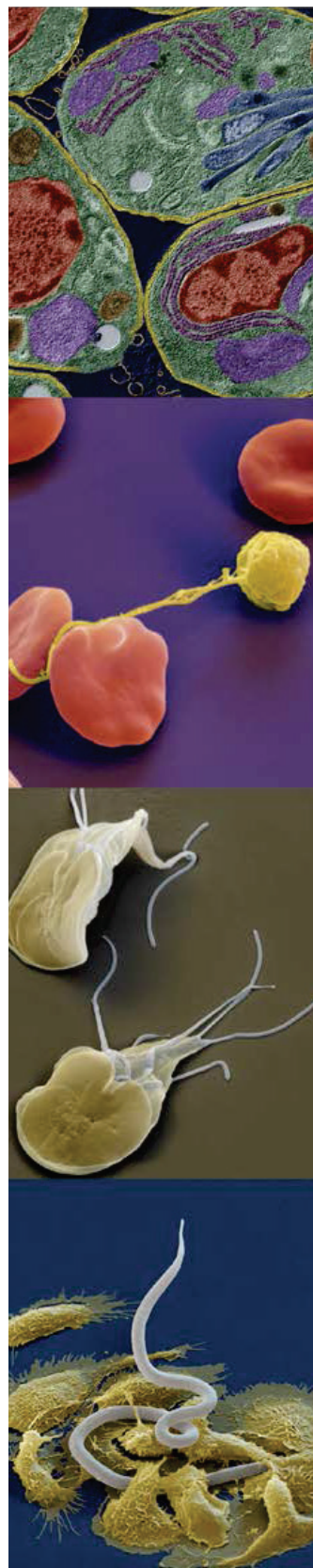
– Felix Goerdeler

### Reflections on challenges and opportunities of online workshops

I was asked to share my experiences with online courses. I am an absolute fan of the endless possibilities of attending digital courses. Corona improved the offer and gave them a high priority.

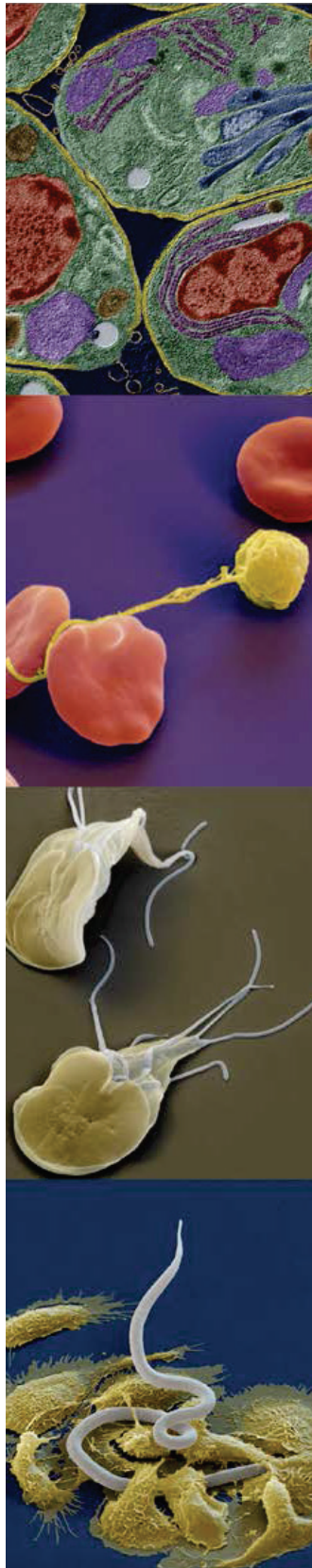
#### **Live or on-demand?**

I have had the best experiences with live sessions. Many lecturers sat when giving their lectures. But one lecturer actually stood at the blackboard and gave his lecture as if it was in a real lecture hall. His talk really had energy. Whether sitting or standing: content is easily conveyed



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digitally. The audience can interact and help shape the session with their questions.

Courses that are not live, but text-/video-based offer the advantage of moving forward at your own pace. And above all, you can choose the time you want to participate. This is a matchless advantage for parents who have to look after their children. However, in courses of this type, the only option of asking questions is via forum/discussion board, i.e. you receive answers with a delay ... often not from the lecturer himself but only from fellow learners - so with a lot of subjunctive. Or in the worst case, your questions will not be answered at all. That's annoying and unsatisfactory without question.

### One example from my experience: datacamp

It can be tricky to find the right course/platform in the jungle of offers. I have had consistently good experiences with datacamp (if this advertising is allowed). Anyone who wants to expand their R knowledge is really well advised to use it. The course structures are clear and varied, which makes it easy to stay on the ball. You can script easily within the session (web-based R interpreter). If you get absolutely stuck, you get hints (with deduction of points, but there is no frustration, because you are helped immediately and you get further). Really addicting!

### The challenges of interacting online

When it comes to networking (online conferences or even digital company contact fairs, or just an online course), everybody gets more reluctant online. When you learn something new, I find it very important to share it with fellow students. Your fellows can't be replaced! Online you can't whisper something into the ear of your desk neighbor, speak with the eyes, or in other words: it is not so easy to get in touch with someone you do not know to share your thoughts. Furthermore, no one will e.g. remember who the diligent questioner was when it is only a digital session (quite unlikely if he/she was actually spending a course in the same room with him/her). I also think that some questions are simply not asked ... the face would reveal doubts, but online it probably remains unseen.

I am absolutely of the opinion that after the pandemic one should try to preserve some of these digital opportunities. In my opinion, online courses cannot completely replace face-to-face courses. But they are a serious addition to the course curriculum!

– Vivian Schüler

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## Berlin Parasitology Seminars (BPS)

**Kerri L. Coon**

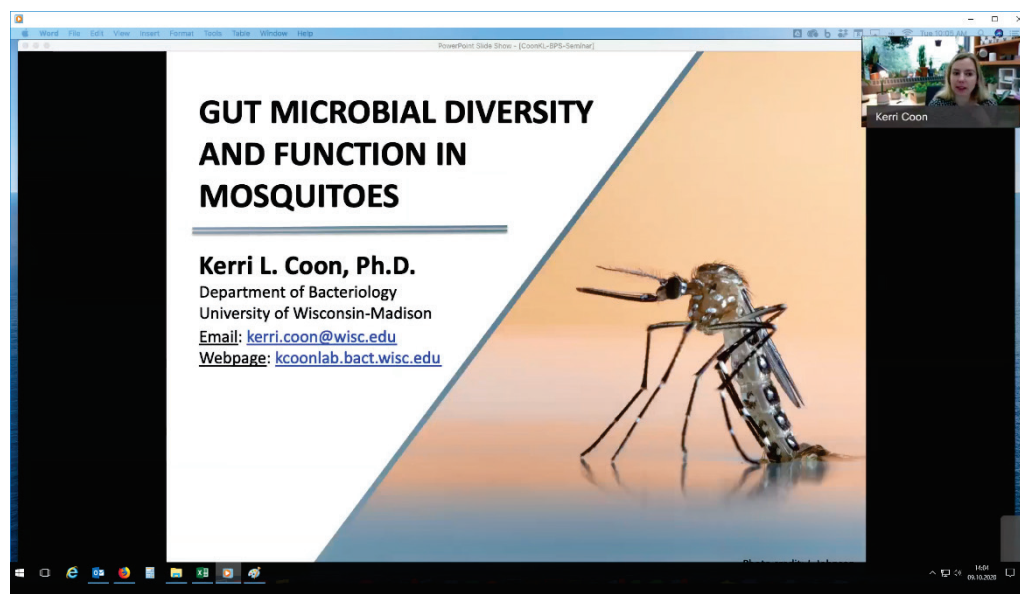
University of Wisconsin-Madison

8<sup>th</sup> September 2020 (online)

After a long break, we restarted the Berlin Parasitology Seminar (BPS) with Kerri L. Coon, Assistant Professor at the University of Wisconsin-Madison in the Department of Bacteriology (<https://kcoonlab.bact.wisc.edu/research/>), who gave an online talk with the title: "Gut microbial diversity and function in mosquitoes".

### **Abstract:**

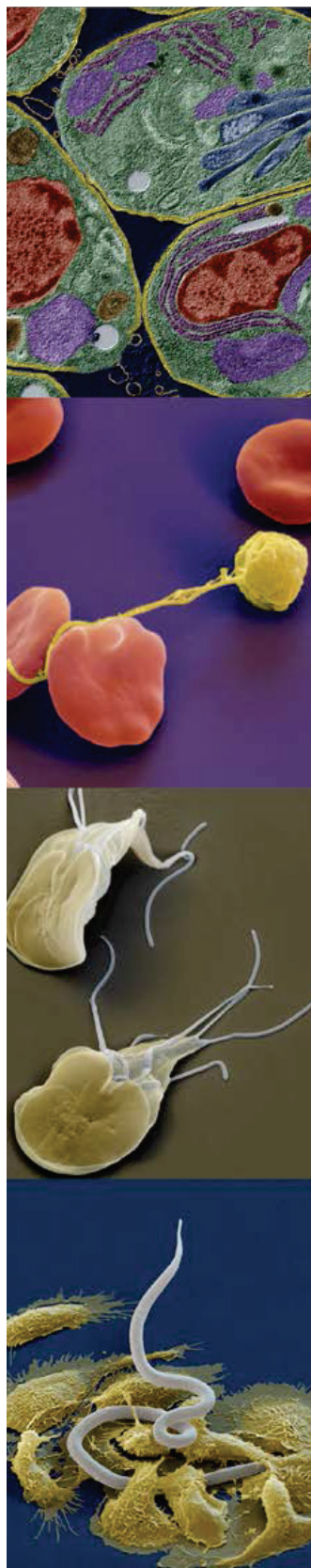
Mosquitoes, transmitting a huge variety of infectious disease, harbor low diversity gut microbial communities comprised primarily of aerobic bacteria. Previous work has shown that larvae of *Aedes aegypti* and several other mosquito species do not develop beyond the first instar in the absence of this gut microbiota. Furthermore, several species of bacteria, including *Escherichia coli*, rescue development of axenic larvae into adults. Recent studies have taken advantage of *E. coli* as a model bacterium to identify the mechanism(s) underlying how bacteria regulate mosquito growth.





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In her fascinating talk, Kerri presented results demonstrating that living bacteria induce gut hypoxia and stabilization of hypoxia-inducible transcription factors in the mosquito host that regulate processes with roles in larval growth and molting.

She also demonstrated the ability of non-bacterial members of the gut microbiota to produce a gut hypoxia signal that promotes mosquito development. Current efforts in her lab focus on the impact of microbial diversity on mosquito growth and the factors underlying microbiota acquisition and homeostasis in mosquitoes.

– Robin Benter

### Jeroen Saeij

University of California – Davis

13<sup>th</sup> October 2020 (online)

On October 13th, Jeroen Saeij, Associate Professor at the department for Pathology, Microbiology and Immunology at the Veterinary Medicine faculty of the University of California Davis, gave a talk on “Identification of novel *Toxoplasma* virulence factors using CRISPR/Cas9-mediated loss-of-function screens”. Dr. Saeij and his lab are most interested in host-parasite interactions and study how *Toxoplasma gondii* modulates its hosts immune system and uses it for its advantage.

In his talk, Jeroen shed some light on his recent publications and detailed how he and his team used CRISPR knock-out screenings to discover new proteins and characterise how *T. gondii* uses these to invade and modulate host cells. One of those discovered proteins is GRA45. In his talk, Jeroen guided us through how he and his team discovered a chaperone like mechanism by GRA45 and its crucial role for the correct localisation and secretion of other GRA proteins, respectively. Moreover, Jeroen and his team discovered that  $\Delta$ gra45 parasites are more susceptible to IFN $\gamma$ -mediated growth inhibition and exhibit reduced virulence in mice.

Sadly, because of travel restrictions due to the SARS-CoV-2 pandemic, Jeroen Saeij was not able to hold the talk in person in Berlin. Instead, the event was held online. However, his talk was well received by many attendees and resulted in a vivid discussion.

– Benedikt Fabian



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### Thomas Jacobs

Bernhard-Nocht Institute for Tropical Medicine, Hamburg

10<sup>th</sup> November 2020 (online)

Dr. Thomas Jacobs from the Protozoan Immunology group at Bernhard-Nocht Institute of Tropical Medicine in Hamburg gave us a fascinating online talk entitled “Immunregulation in Malaria: A balance between protection and pathology” where he shared with us a range of immunoregulatory mechanisms that take place during a *Plasmodium* infection.

As an expert in protozoan immunology, it comes as no surprise that his laboratory group studies a wide range of clinically important vector-borne parasites and the cellular immunity involved during the infections. In particular, their main interest is investigating the function of co-inhibitory signals on T cells during malaria, while other research interests include the cellular immunity associated with Chagas disease and leishmaniasis.

Due to the current COVID-19 lockdown restrictions, we were unfortunately unable to host Dr. Thomas Jacobs in person for the Berlin Parasitology Seminar series this month. But nonetheless, it was definitely an enlightening seminar that has brought us a lot of insight into his field.

– Calvin Hon

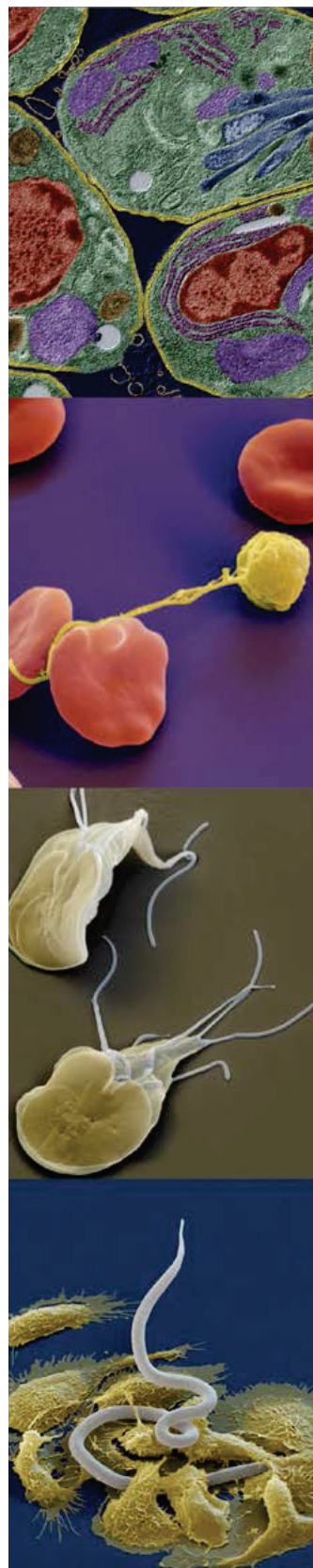
### Role Models Seminars

#### Paul Selzer

Boehringer Ingelheim

15<sup>th</sup> September 2020 (online)

Prof. Dr. Paul Selzer, Head of Molecular Discovery at Boehringer Ingelheim Animal Health and simultaneously Professor for biochemistry at the University Tübingen, has been working on parasitic questions since 1983. Prof. Selzer has therefore been invited to the Role Models seminar series where he gave the talk „Antiparasitics: A Personal Perspective“. He provided an extensive overview of his career pathway and the projects he worked on during his lifetime. His research mainly focuses on drug design and discovery based on bio- and chemoinformatics. The talk was followed by an informal career discussion via Webex. Prof. Dr.



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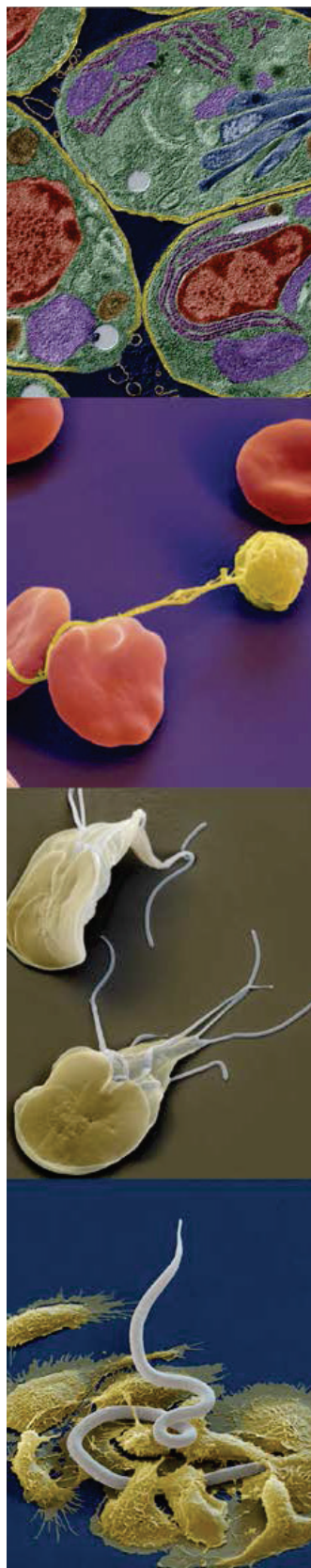
Selzer gave us the advice that conversations can often take you much further in your career than collecting certificates.

– Natalie Jakobs and Irina Diekmann

### Assessment center, November 1-6, 2020

At the beginning of 2020, we started to prepare the assessment center (AC) 2020. Here, we wanted to recruit the third (and sadly final) generation of GRK 2046 PhD students. Shortly after the first lockdown was decreed due to the coronavirus, we were still confident to be back to normal status by the end of 2020, when the AC was planned to take place. We were wrong. The next months turned out to consist of ups and downs in organizing, not knowing whether the AC could be in Berlin in presence or ONLINE. Fortunately, we started early enough to follow both ways. And ONLINE won the first prize. It was difficult to organize, because we never did it before this way. How to compensate the major drawback that the candidates could not walk around Berlin themselves and meet all relevant scientists during an easy-going dinner? How to make sure that the (online) technique is working properly? How to organize social contacts?

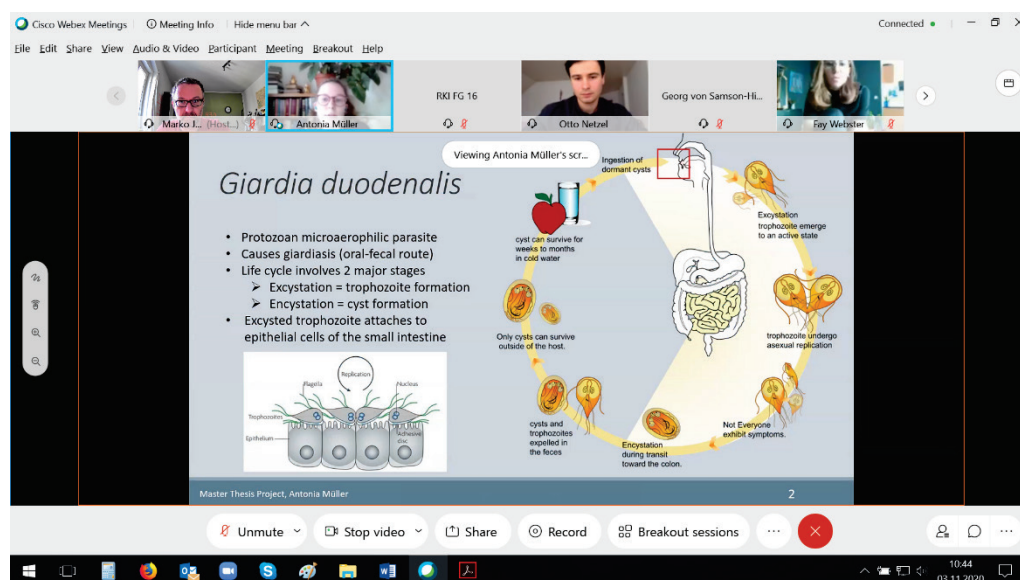
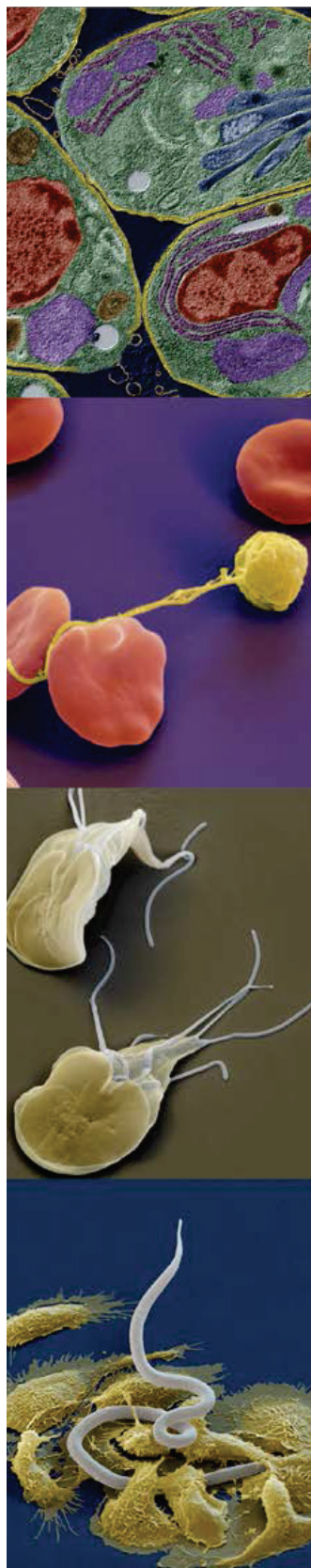
When finally the schedule was finished, many people had concerns like “It cannot work like this!”. However, after the AC the author was very glad that many sceptical people just turned out to be quite happy and satisfied with the concept. In the welcome meeting, the GRK 2046 coordinator showed a nice video about Berlin and the different GRK locations. We were very happy to use the FUB-provided WebEx platform, which was working well with minor problems (for which only the bad WIFI reception was to blame, I swear!). Outstanding highlights were the social online meetings of the candidates, dinner with the PIs and supper with the current PhD students. We brought together candidates and scientists in breakout rooms, swapping candidates from time to time to different rooms. The surprise who awaits me in the next room was well accepted by all participants. Beer, food, shots of whiskey, and more were consumed during the meetings.





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Finally, the AC ONLINE was a success. New extraordinary PhD students for 12 projects were selected and will be welcomed to Berlin in April 2021. For 3 projects, we just started the 2<sup>nd</sup> call and hope to find 3 more excellent PhD students in January's AC.

– Marko

## Publications

### Canine Dracunculus Nematode Infection, Toledo, Spain

**Diekmann I.**, Alnassan AA., Globokar M., Pantchev N., Kurzrock L., Hernandez L., Lopez J., Ruano R., Herrero S., **von Samson-Himmelstjerna G.**, Krücken J.

*Emerg Infect Dis.* Aug;26(8):1860-1863 (2020)  
doi: 10.3201/eid2608.201661.

#### **Abstract:**

A fragment of a Dracunculus-like worm was extracted from the hind limb of a 2-year-old dog from Toledo, Spain. Cytochrome oxidase I and rRNA sequences confirmed an autochthonous mammalian Dracunculus worm infection in Europe. Sequence analyses suggest close relation to a parasite obtained from a North American opossum.

### Fluorescent bead-based serological detection of *Toxoplasma gondii* infection in chickens

**Fabian B.T.**, Hedar F., Koethe M., Bangoura B., Maksimov P., Conraths F.J., Villena I., Aubert D., **Seeber F.**, Schares G.

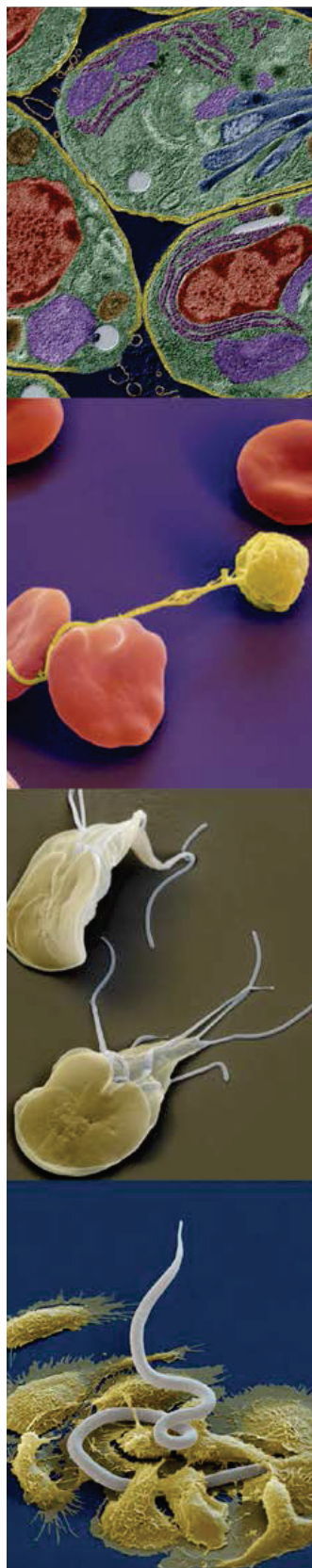
*Parasit Vectors*. Jul 31;13(1):388 (2020)  
doi: 10.1186/s13071-020-04244-6

#### **Abstract:**

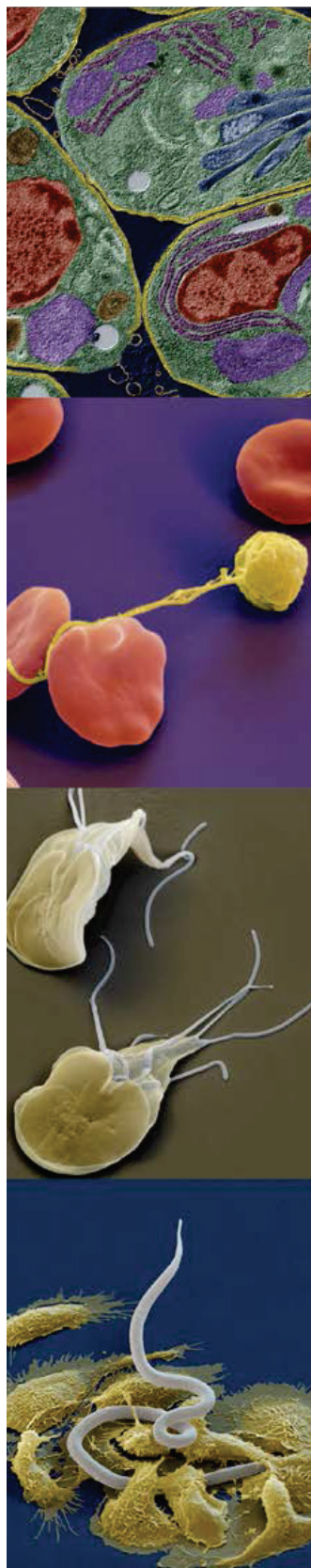
Background: Free-ranging chickens are often infected with *Toxoplasma gondii* and seroconvert upon infection. This indicates environmental contamination with *T. gondii*.

Methods: Here, we established a bead-based multiplex assay (BBMA) using the Luminex technology for the detection of *T. gondii* infections in chickens. Recombinant biotinylated *T. gondii* surface antigen 1 (TgSAG1bio) bound to streptavidin-conjugated magnetic Luminex beads served as antigen. Serum antibodies were detected by a fluorophore-coupled secondary antibody. Beads of differing color codes were conjugated with anti-chicken IgY or chicken serum albumin and served for each sample as an internal positive or negative control, respectively. The assay was validated with sera from experimentally and naturally infected chickens. The results were compared to those from reference methods, including other serological tests, PCRs and bioassay in mice.

Results: In experimentally infected chickens, the vast majority (98.5%,  $n = 65/66$ ) of birds tested seropositive in the BBMA. This included all chickens positive by magnetic-capture PCR (100%,  $n = 45/45$ ). Most, but not all inoculated and TgSAG1bio-BBMA-positive chickens were also positive in two previously established TgSAG1-ELISAs (TgSAG1-ELISASL,  $n = 61/65$ ; or TgSAG1-ELISASH,  $n = 60/65$ ), or positive in an immunofluorescence assay (IFAT,  $n = 64/65$ ) and in a modified agglutination test (MAT,  $n = 61/65$ ). All non-inoculated control animals ( $n = 28/28$ , 100%) tested negative. In naturally exposed chickens, the TgSAG1bio-BBMA showed a high sensitivity (98.5%; 95% confidence interval, CI: 90.7-99.9%) and specificity (100%; 95% CI: 85.0-100%) relative to a reference standard established using ELISA, IFAT and MAT. Almost all naturally exposed chickens that were positive in bioassay or by PCR tested positive in the TgSAG1bio-BBMA (93.5%; 95% CI: 77.1-98.9%), while all bioassay- or PCR-negative chickens remained negative (100%; 95% CI: 85.0-100%).







**Conclusions:** The TgSAG1bio-BBMA represents a suitable method for the detection of *T. gondii* infections in chickens with high sensitivity and specificity, which is comparable or even superior to other tests. Since assays based on this methodology allow for the simultaneous analysis of a single biological sample with respect to multiple analytes, the described assay may represent a component in future multiplex assays for broad serological monitoring of poultry and other farm animals for various pathogens.

### Targeting and Inhibiting *Plasmodium falciparum* Using Ultra-small Gold Nanoparticles

Varela-Aramburu S., Ghosh C., **Goerdeler F.**, Priegue P., **Moscovitz O.**, **Seeberger P.H.**

*ACS Appl. Mater. Interfaces*; 12:43380–43387 (2020)  
doi: 10.1021/acsami.0c09075

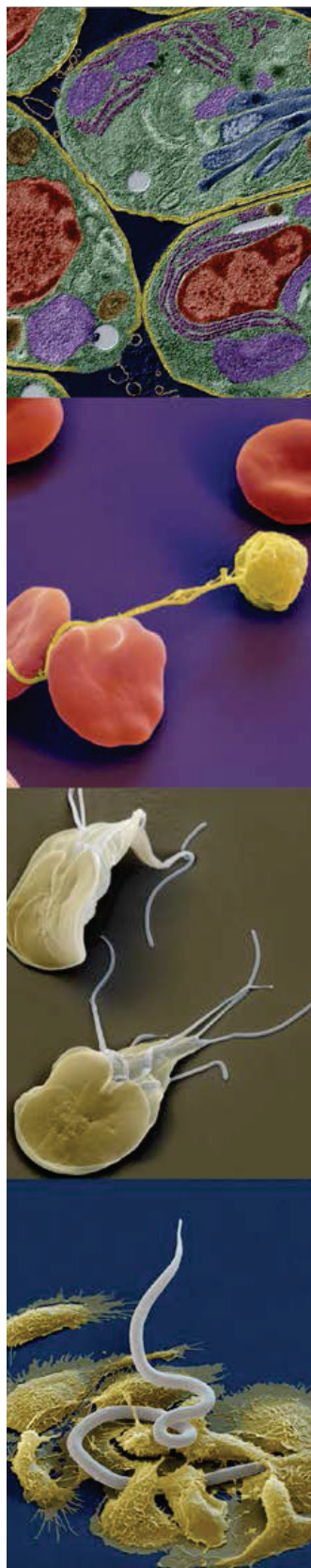
#### **Abstract:**

Malaria, a mosquito-borne disease caused by *Plasmodium* species, claims more than 400,000 lives globally each year. The increasing drug resistance of the parasite renders the development of new anti-malaria drugs necessary. Alternatively, better delivery systems for already marketed drugs could help to solve the resistance problem. Herein, we report glucose-based ultra-small gold nanoparticles (Glc-NCs) that bind to cysteine-rich domains of *Plasmodium falciparum* surface proteins. Microscopy shows that Glc-NCs bind specifically to extracellular and all intra-erythrocytic stages of *P. falciparum*. Glc-NCs may be used as drug delivery agents as illustrated for ciprofloxacin, a poorly soluble antibiotic with low antimalarial activity. Ciprofloxacin conjugated to Glc-NCs is more water-soluble than the free drug and is more potent. Glyco-gold nanoparticles that target cysteine-rich domains on parasites may be helpful for the prevention and treatment of malaria.

### Trilateral relationship: *Ascaris*, microbiota, and host cells

**Midha, A.**; Ebner, F.; Schlosser-Brandenburg, J.; **Rausch, S.**; **Hartmann, S.**

*Trends in parasitology*, S. 2049 (2020)  
doi: 10.1016/j.pt.2020.09.002



### Abstract:

Ascariasis is a globally spread intestinal nematode infection of humans and a considerable concern in pig husbandry. *Ascaris* accomplishes a complex body migration from the intestine via the liver and lung before returning to the intestine. Tissue migration and the habitat shared with a complex microbial community pose the question of how the nematode interacts with microbes and host cells from various tissues. This review addresses the current knowledge of the trilateral relationship between *Ascaris*, its microbial environment, and host cells, and discusses novel approaches targeting these interactions to combat this widespread infection of livestock and man.

### Eosinophils are dispensable for the regulation of IgA and Th17 responses in *Giardia muris* infection

Yordanova, I. A.; Lamatsch, M.; Kühl, A. A.; Hartmann, S.; Rausch, S.

*Parasite Immunol*, S. e12791 (2020)

doi: 10.1111/pim.12791

### Abstract:

**Aims:** IgA and Th17 responses are pivotal for the control of *Giardia* infections. Eosinophils support IgA class switching, the survival of intestinal IgA<sup>+</sup> plasma cells at steady state and can control Th17 activity in the small intestine. To see whether eosinophils regulate adaptive immune responses during giardiasis, we investigated *Giardia muris* infections in wild-type BALB/c and eosinophil-deficient  $\Delta$ dblGATA-1 mice.

**Methods and results:** Infected  $\Delta$ dblGATA-1 mice did not differ markedly in parasite control from wild-type mice. Confirming previous studies, naive  $\Delta$ dblGATA-1 mice displayed diminished IgA<sup>+</sup> B cell frequencies in Peyer's patches. However, IgA class switching and intestinal IgA secretion in response to *G. muris* infection were comparable in wild-type BALB/c and  $\Delta$ dblGATA-1 mice. Both strains displayed similarly low intestinal Th17 responses, accompanied by a mild expansion of type 3 innate lymphoid cells (ILC3).

**Conclusions:** Contrasting previous reports on overt small intestinal Th17 activity in eosinophil-deficient mice, IL-17A production is kept in check in the absence of eosinophils during *Giardia* infection. Suboptimal homeostatic IgA responses in the absence of eosinophils are transiently fostered in infected mice and the maintenance of IgA<sup>+</sup> plasma cells appears to be restored during persisting *Giardia* infection.



### Rapid Gastrointestinal Passage May Protect *Bombus terrestris* from Becoming a True Host for *Nosema ceranae*

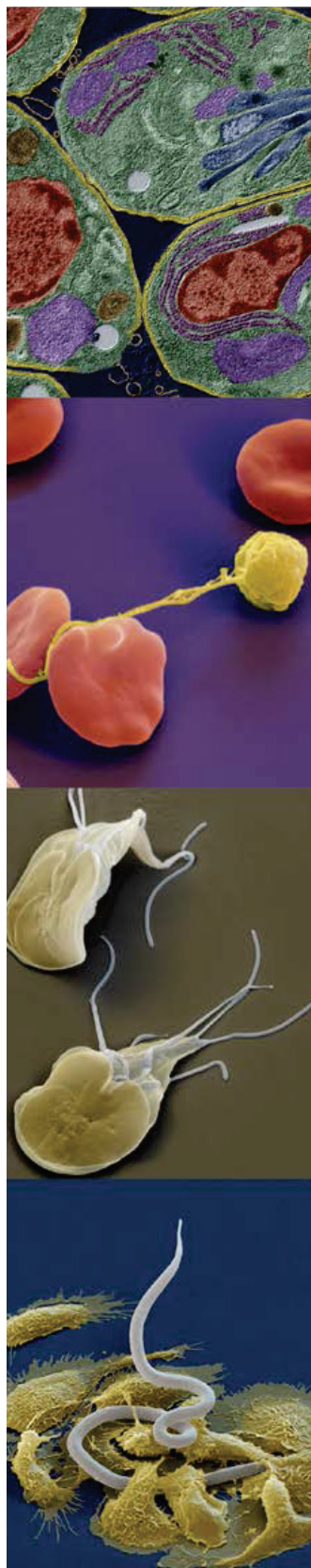
Gisder S., Horschler L., Pieper F., **Schüler V.**, Šima P., **Genersch E.**

*Appl Environ Microbiol*; 86:e00629-20 (2020)  
doi: 10.1128/AEM.00629-20

#### **Abstract:**

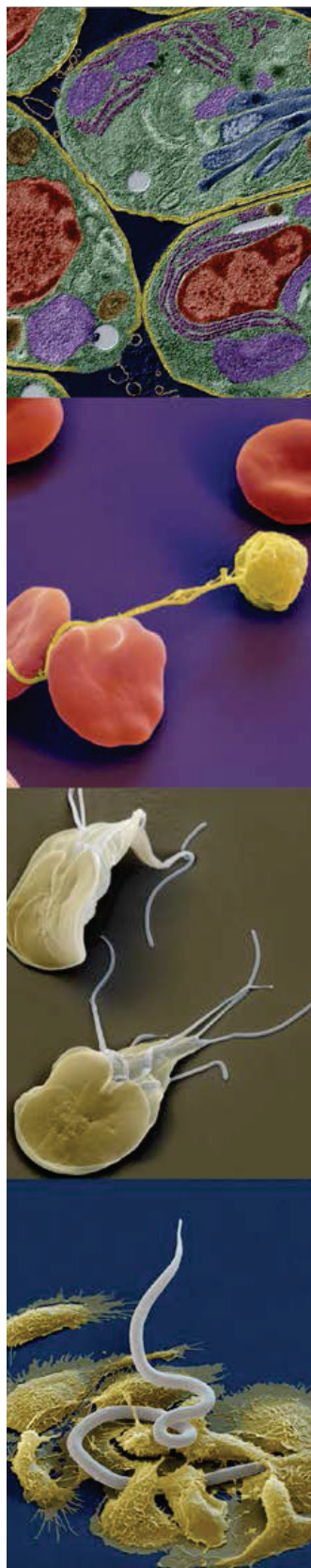
Pollination provided by managed honey bees as well as by all the wild bee species is a crucial ecosystem service contributing to the conservation of biodiversity and human food security. Therefore, it is not only the health status of honey bees but also the health status of wild bees that concerns us all. In this context, recent field studies suggesting interspecies transmission of the microsporidium parasite *Nosema ceranae* from honey bees (*Apis mellifera*) to bumblebees (*Bombus* spp.) were alarming. On the basis of these studies, *N. ceranae* was identified as an emerging infectious agent (EIA) of bumblebees, although knowledge of its impact on its new host was still elusive. In order to investigate the infectivity, virulence, and pathogenesis of *N. ceranae* infections in bumblebees, we performed controlled laboratory exposure bioassays with *Bombus terrestris* by orally inoculating the bees with infectious *N. ceranae* spores. We comprehensively analyzed the infection status of the bees via microscopic analysis of squash preparations, PCR-based detection of *N. ceranae* DNA, histology of Giemsa-stained tissue sections, and species-specific fluorescence in situ hybridization. We did not find any evidence for a true infection of bumblebees by *N. ceranae*. Through a series of experiments, we ruled out the possibility that spore infectivity, spore dosage, incubation time, or age and source of the bumblebees caused these negative results. Instead, our results clearly demonstrate that no infection and production of new spores took place in bumblebees after they ingested *N. ceranae* spores in our experiments. Thus, our results question the classification of *N. ceranae* as an emerging infectious agent for bumblebees.

**IMPORTANCE:** Emerging infectious diseases (EIDs) pose a major health threat to both humans and animals. EIDs include, for instance, those that have spread into hitherto naive populations. Recently, the honey bee-specific microsporidium *Nosema ceranae* has been detected by molecular methods in field samples of bumblebees. This detection of *N. ceranae* DNA in bumblebees led to the assumption that *N. ceranae* infections represent an EID of bumblebees and resulted in speculations on the role of this pathogen in driving bumblebee declines. In order to address the issue of whether *N. ceranae* is an emerging infectious agent for bumblebees, we experimentally analyzed host susceptibility and



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pathogen reproduction in this new host-pathogen interaction. Surprisingly, we did not find any evidence for a true infection of *Bombus terrestris* by *N. ceranae*, questioning the classification of *N. ceranae* infections as EIDs of bumblebees and demonstrating that detection of microsporidian DNA does not equal detection of microsporidian infection.

### The P-glycoprotein repertoire of the equine parasitic nematode *Parascaris univalens*

**Gerhard, A.P.; Krücken, J.; Heitlinger, E.; Janssen, I.J.; Basiaga, M., Kornaś, S.; Beier, C.; Nielsen, M.K.; Davis, R.E.; Wang, J.; von Samson-Himmelstjerna, G.**

*Sci. Rep.*; Volume 10, Article no.: 13586 (2020)  
doi: 10.1038/s41598-020-70529-6

#### **Abstract:**

P-glycoproteins (Pgp) have been proposed as contributors to the widespread macrocyclic lactone (ML) resistance in several nematode species including a major pathogen of foals, *Parascaris univalens*. Using new and available RNA-seq data, ten different genomic loci encoding Pgps were identified and characterized by transcriptome-guided RT-PCRs and Sanger sequencing. Phylogenetic analysis revealed an ascarid-specific Pgp lineage, Pgp-18, as well as two paralogues of Pgp-11 and Pgp-16. Comparative gene expression analyses in *P. univalens* and *Caenorhabditis elegans* show that the intestine is the major site of expression but individual gene expression patterns were not conserved between the two nematodes. In *P. univalens*, PunPgp-9, PunPgp-11.1 and PunPgp-16.2 consistently exhibited the highest expression level in two independent transcriptome data sets. Using RNA-Seq, no significant upregulation of any Pgp was detected following in vitro incubation of adult *P. univalens* with ivermectin suggesting that drug-induced upregulation is not the mechanism of Pgp-mediated ML resistance. Expression and functional analyses of PunPgp-2 and PunPgp-9 in *Saccharomyces cerevisiae* provide evidence for an interaction with ketoconazole and ivermectin, but not thiabendazole. Overall, this study established reliable reference gene models with significantly improved annotation for the *P. univalens* Pgp repertoire and provides a foundation for a better understanding of Pgp-mediated anthelmintic resistance.



# GRK 2046 Newsletter

## December 2020

### CD4<sup>+</sup> Th immunogenicity of the *Ascaris* spp. secreted products

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#### **Abstract:**

*Ascaris spp.* is a major health problem of humans and animals alike, and understanding the immunogenicity of its antigens is required for developing urgently needed vaccines. The parasite-secreted products represent the most relevant, yet complex (>250 proteins) antigens of *Ascaris spp.* as defining the pathogen-host interplay. We applied an in vitro antigen processing system coupled to quantitative proteomics to identify potential CD4<sup>+</sup> T<sub>h</sub> cell epitopes in *Ascaris*-secreted products. This approach considerably restricts the theoretical list of epitopes using conventional CD4<sup>+</sup> T<sub>h</sub> cell epitope prediction tools. We demonstrate the specificity and utility of our approach on two sets of candidate lists, allowing us identifying hits excluded by either one or both computational methods. More importantly, one of the candidates identified experimentally, clearly demonstrates the presence of pathogen-reactive T cells in healthy human individuals against these antigens. Thus, our work pipeline identifies the first human T cell epitope against *Ascaris spp.* and represents an easily adaptable platform for characterization of complex antigens, in particular for those pathogens that are not easily amenable for in vivo experimental validation.

### **Merry Christmas**

I know restrictions in social contacts due to the SARS-CoV-2 will somehow change the usual Christmas celebrations and everything else. However, I wish everyone a Merry Christmas and a Happy New Year. See you all in 2021 (maybe in person).

– Marko

