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https://www.vetmed.fu-berlin.de/en/einrichtungen/sonstige/grk2046/application_2020

Application platform; please visit:

https://www.drs.fu-berlin.de/user/register?field_i_want_to_apply_for=732

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https://www.vetmed.fu-berlin.de/en/einrichtungen/sonstige/grk2046/index.html

For further questions, please refer to the coordinator (Marko): grk2046@fu-berlin.de

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A3

Supervisors: Peter H. Seeberger, Oren Moscovitz

Research Group: Biomolecular Systems, Glycan-Targeted Therapeutics Group

Address: Max Planck Institute of Colloids and Interfaces, Freie Universität Berlin,
Institute of Chemistry and Biochemistry, Arnimallee 22, 14167 Berlin

Characterizing the biological role of glycosylation in *Plasmodium falciparum* communication by extracellular vesicles

Cell-cell communication by extracellular vesicles (EVs) secretion is a phenomenon that was described in a wide range of organisms, from humans and plants to bacteria and protozoan parasites. EVs carry biomolecules such as proteins, lipids, and nucleic acids, between adjacent cells, and participate in a diverse and wide range of biological activities as cell signaling and quorum sensing. The content and size of secreted EVs is a dynamic process, which changes due to different extra- and intracellular signals and differs between cells and organisms. Although EVs biology is extensively studied for over a decade, the involvement and specific role of glycans in EVs secretion, uptake, and downstream signaling were not fully elucidated yet.

Malaria is a devastating parasitic disease caused by species of the protozoan parasite Plasmodium. The disease threatens 40% of the world's population and claims more than 600.000 lives each year. To date, the role of host or parasite glycans that are membrane-embedded as glycolipids, or carried on glycoproteins in Plasmodium derived EVs, is still a mystery that was hardly investigated.

By combining advanced biochemical techniques and synthetic glycans arrays, with lectins and specific glycan-binding nanobodies that were recently developed in-lab, we aim to shed light on the unique role of glycans in different biological aspects of Plasmodium derived EVs. We will identify and investigate glycan contribution to Evs mediated communication between parasites during the different stages of the asexual blood-stage development. Additionally, we will inspect the influence of EVs glycans on immune system response and overall virulence of *Plasmodium* spp *in vitro* and *in vivo*.

http://www.mpikg.mpg.de/en/bs

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A5

Supervisor: Jürgen Krücken

Research Group: Institute for Parasitology and Tropical Veterinary Medicine

Address: Institute for Parasitology, Freie Universität Berlin,
Robert-von-Ostertag-Str. 7-13, 14163 Berlin

Characterization of MDR pathways in trichostrongyloid parasitic nematodes of ruminants

Gastrointestinal parasitic nematodes (GINs) are ubiquitous pathogens of humans, pets and livestock with severe impact on public and animal. Without available vaccinations, treatment with anthelmintics is the major weapon to limit this impact and is essential for sheep and cattle production. However, frequent treatments and a limited number of available drug classes have selected highly drug-resistant GIN populations often showing multi-drug resistance (MDR) which involves pathways for detoxification of xenobiotics. In previous projects we have characterized and identified various transporters and enzymes (cytochrome P450, FADH-monooxygenases, glutathione-S-transferases) using RNAseq and expression in yeast or the model nematode *Caenorhabditis elegans*. This project will quantify the effects of individual and combined enzymes and transporters on the effects of levamisole, albendazole, ivermectin and moxidectin to analyze their interaction in MDR using targeted integration by CRISPR/Cas-9.

https://www.vetmed.fu-berlin.de/en/einrichtungen/institute/we13/index.html

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A6

Supervisor: Alyssa Ingmundson

Research Group: Molecular parasitology

Address: Department of Molecular Parasitology, Humboldt University,
Philippstr 13, Haus 14

Characterizing host Rab GTPases involved in Plasmodium liver-stage development

Plasmodium undergo a single extensive growth phase in the liver at the onset of infection. The parasite population and the parasitophorous vacuole (PV) in which they reside expand rapidly during this developmental stage. We hypothesize that the *Plasmodium* PV intercepts host vesicular transport to obtain necessary lipids and other metabolites. This project will investigate the interactions between the PV and host through the study of host Rab GTPases, which label distinct membranes and regulate membrane transport and fusion. Rab proteins are attractive candidates for this analysis because many pathogens directly usurp host Rab proteins to establish an intracellular niche, several established tools can be used to interrogate the function of specific Rabs, and host Rabs have been shown to influence susceptibility to infection. The project aims to uncover host pathways that contribute to successful parasite development and reveal how these pathways impact host susceptibility to infection.

https://www.biologie.hu-berlin.de/en/gruppenseiten-en/molpara-en/standardseite?set_language=en

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B1

Supervisor: Katja Müller, Kai Matuschewski

Research Group: Molecular parasitology

Address: Department of Molecular Parasitology, Humboldt University,
Philippstr 13, Haus 14

Immune correlates of protective immunity against Plasmodium infections

Generation of lasting protection against malaria remains a major challenge. Immune recognition and vaccine induced protection during *Plasmodium* liver development will be studied in a preclinical murine malaria model. Experimental genetics, analysis of a wildlife *Plasmodium*-bat association, immunological assays and vaccination protocols are complementary approaches that will be employed to study the critical roles of anti-sporozoite antibodies, cytotoxic T cells and display of sporozoite antigens in elimination of transmission stages and infected hepatocytes. Live attenuated vaccine strains will be compared to identify signatures of immune protection. Exchange of immunodominant antigens and expression of candidate blood stage antigens in transgenic parasites can inform vaccine development and might improve malarial vaccine efficacy. Together, these studies will provide critical insights into vaccine-induced and naturally acquired immunity against malaria.

https://www.biologie.hu-berlin.de/en/gruppenseiten-en/molpara-en/standardseite?set_language=en

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B3

ROBERT KOCH INSTITUT

Supervisor: Toni Aebischer

Research Group: FG16 Mycotic and parasitic agents and mycobacteria

Address: Robert Koch Institute, FG16, Seestraße 10, 13353 Berlin

Giardia duodenalis – interaction with natural human tissue stem cell derived epithelium to decipher the role of the Cystic Fibrosis Transduction receptor (CFTR) in pathogenesis

Giardia duodenalis (*Gd*) designates a species complex of protozoan parasites causing acute and chronic intestinal disease. We have established unique stem-cell derived organoid models to study parasite-host interaction that depend on host genetic background and determinants such as cystic fibrosis mutations (CF). The hypothesis to be tested in this project that CF-related functional differences in these epithelia will impact the effect of *Gd* colonization, alone or in combination with other microbial/microbiota related factors.

The experimental approach to test these hypotheses will exploit an organoid-derived, compartmentalized transwell system established for infection experiments. Read outs on barrier and epithelial function will be based on electrophysiology, transcriptomics of host and parasite responses and advanced microscopic analyses. Students should therefore be keen to embark on a highly multidisciplinary project.

https://www.rki.de/EN/Content/Institute/DepartmentsUnits/InfectDiseases/Div16/Div16_node.html

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B4

Supervisor: Susanne Hartmann

Research Group: Institute of Immunology

Address: Institute of Immunology, Freie Universität Berlin,
Robert-von-Ostertag-Str. 7-13, 14163 Berlin

Enteric coinfections and its consequences on mucosal immune challenges

Co-infections with pathogens impose major challenges to the host immune system. Immune cells as gatekeepers sense antigens of invading pathogens and react e.g. by cytokine production. An adaptation of immune cell responses depends on pathogen nature, dose and succession. Our previous work on the influence of pathogens controlled by opposing immune responses showed that a previous *Toxoplasma* infection limits Th2 immunity and directs residual anti-helminth responses to inappropriate Th1 reactions. We now aim to study two enteric nematode infections, one being strictly enteric and the other one migrating through the body before residing in the intestine. Focus of the project is to decipher the impact of the infections and coinfections on different mucosal sites: the gut versus the lung. Questions are: how and by which mechanisms are mucosal lung immune cells affected by the enteric infections and what impact do they have on other lung challenges such as allergic reactions?

https://www.vetmed.fu-berlin.de/en/einrichtungen/institute/we06/index.html

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B5

Supervisor: Sebastian Rausch

Research Group: Institute of Immunology

Address: Institute of Immunology, Freie Universität Berlin,
Robert-von-Ostertag-Str. 7-13, 14163 Berlin

Host genotype and microbiota affect protective immunity to co-infections with intestinal parasites

Intestinal nematodes and *Giardia* parasites are controlled by distinct immune responses, alter the gut microbiota and promote immune regulatory activities. Cross-regulation by opposing stimuli, prevents overtly biased reactions, but also limits pathogen control. Under laboratory conditions, protective immunity to both nematode and *Giardia* species is readily achieved, whereas individuals frequently experience coinfections and often display poor immunity in natural systems.

This project will hence investigate the development of protective immunity to nematode/*Giardia* single and coinfections depending on I) host genotype, II) microbiome signature, and III) intervention with regulatory/effector profiles and evaluate the robustness of the experimental findings in a natural system.

- **Murine nematode/*Giardia* infection models**
- **Immunological techniques**
  FACS, *in vivo* imaging, multiplexing etc.
  Cell depletion, transfer and tracking; reporter/knock out models
- **Microbiota/natural systems** (collaborative work)

https://www.vetmed.fu-berlin.de/en/einrichtungen/institute/we06/index.html

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C1

Supervisors: Bettina Wachter, Gábor Czirják, Heribert Hofer

Research Group: Department of Evolutionary Ecology

Address: Leibniz Institute for Zoo and Wildlife Research (IZW),
Alfred-Kowalke-Str. 17, 10315 Berlin

Apicomplexan parasites, immunity and its link to life history states in cheetahs

This project will investigate parasite load and immune responses in a genetically monomorphic carnivore, the cheetah. Little is known about parasite susceptibility of free-ranging threatened wildlife species. Cheetahs have a low level of variability at fitness-related immune genes (MHC) and are highly susceptible to infectious diseases when kept in zoos but not in the wild. This project will analyze samples collected from free-ranging cheetahs in Namibia and examine how apicomplexan infections and parasite load depend on reproductive status, territorial status and group size of cheetahs. It will further examine the extent to which other components of the immune system can compensate the low MHC variability. Some protocols for testing particular components of the immune system of the cheetahs are already developed, others will be developed during this project. An important part of the project will also be the management of several thousand samples from several hundred cheetahs.

http://www.izw-berlin.de/en/departement-of-evolutionary-ecology.html

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C3

Supervisor: Frank Seeber

Research Group: FG16 Mycotic and parasitic agents and mycobacteria

Address: Robert Koch Institute, FG16, Seestraße 10, 13353 Berlin

Comparative analysis of intestinal host responses from wild rodents upon co-infection with Toxoplasma gondii and Giardia sp.

The intestine is the entry port or replicative niche for *Toxoplasma gondii* and *Giardia sp*., respectively; thus, co-infection will influence the course or establishment of infection reciprocally, but this has not been studied. We established co-cultures of the two parasites in intestinal organoids (IOs) from inbred lab mice and the vole *Myodes glareolus* (a more natural rodent host for both parasites). Using the two *in vitro* systems, we want to study the following:

What role do innate immune responses play during co-infection of IOs? How do they differ between both hosts? How does co-culture of infected IOs with immune cells influence the course of infection? How do these aspects differ between parasites stages of *T. gondii*? Finding answers will be approached by transcriptomics, live microscopy, cytokine assays etc. using transgenic parasites.

A second focus is the optimization of conditions that allow the *in vitro* generation of *T. gondii* oocysts in IOs, based on preliminary own work and literature reports.

https://www.rki.de/EN/Content/Institute/DepartmentsUnits/InfectDiseases/Div16/Div16_node.html

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C4

Supervisors: Heribert Hofer, Gábor Czirják, Sarah Benhaiem

Research Group: Department of Ecological Dynamics

Address: Leibniz Institute for Zoo and Wildlife Research (IZW),
Alfred-Kowalke-Str. 17, 10315 Berlin

Intrinsic and extrinsic determinants of helminth parasite infections of female hyenas

The successful candidate will investigate the influence of immune gene diversity and parasite infection on components of Darwinian fitness in individually known spotted hyenas. Long-term individual data are available on a range of relevant phenotypic traits as well as components of Darwinian fitness. Using banked samples, the candidate will determine the immune genotypes of known spotted hyenas, assess parasite loads and immune response, to extend existing preliminary data. Information on immune genotypes, measures of relevant phenotypic traits and components of fitness will be curated into a master data base for extensive analyses. Experience of genetic analyses, parasites, immunology, establishing large data sets and statistical analyses would be helpful. A good standard of written and spoken English is required. This project is based within the Serengeti Spotted Hyena Research Team in the Dept of Ecological Dynamics at the IZW, an interdisciplinary institute to improve conservation.

http://www.izw-berlin.de/en/departement-of-ecological-dynamics.html

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C5

Supervisor: Georg von Samson-Himmelstjerna, Jürgen Krücken

Research Group: Institute for Parasitology and Tropical Veterinary Medicine

Address: Institute for Parasitology, Freie Universität Berlin,
Robert-von-Ostertag-Str. 7-13, 14163 Berlin

Ecological interdependencies and bio/pathological consequences of equine multi-species infection complexes

The cyathostomins are parasitic nematodes and represent the by far most prevalent pathogens of horses. They consist of 50 morphologically characterized species and in individual hosts sometimes over 20 species occur simultaneously. They thus can be regarded as a uniquely divers group of closely related metazoan organisms evolved to populate the same defined habitat. They are also considered to be the clinically most important equine parasites since they may cause severe disease such as acute diarrhea, weight loss and even death. During previous projects, significant progress has been made concerning proteomic and molecular species identification, population structure and relevance of geographical background. Employing next-generation-sequencing, bioinformatics and MALDI-TOF approaches, this project will now for the first time embark to study another layer of co-evolution by comparing the cyathostomin community composition on a species-specific level with the prevailing microbiome.

https://www.vetmed.fu-berlin.de/en/einrichtungen/institute/we13/index.html

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C6

Supervisors: Elena Levashina

Research Group: Vector Biology Unit at MPIIB

Address: Max Planck Institute for Infection Biology, Charitéplatz 1, 10117 Berlin

Environmental microbes and Plasmodium transmission

Transmission of malaria parasites by mosquito vectors is crucial for disease epidemics. However, the role of such environmental factors as microbial communities in establishment of vector competence are not well understood. This project is based on previous studies in the Unit that investigated immune and metabolic factors at the bacteria – mosquito vector interplay. The preliminary data points to extensive metabolic exchanges between certain bacteria species and mosquitoes that shape development of human malaria *P. falciparum* parasites. The major question of this project is whether we can design microbial communities that will render mosquitoes refractory to malaria parasites. The applicant will design microbial communities, colonize mosquitoes and perform experimental infections with *P. falciparum*. To identify molecular and metabolic interactions between the mosquitoes, parasites and microbiota, the applicant will perform metabolic characterization of these interactions.

https://www.mpiib-berlin.mpg.de/research/vector_biology

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C7

Supervisor: Frank Mockenhaupt

Research Group: Institute of Tropical Medicine and International Health

Address: Charité - Universitätsmedizin Berlin, Augustenburger Platz 1, 13353 Berlin

Impact of *Ascaris-Plasmodium* co-infection on antimalarial treatment outcome, re-infection and antimalarial drug resistance

Immunomodulation induced by soil-transmitted helminths (STHs) counteracts Th1 responses, which are needed to control *Plasmodium falciparum* but also contribute to pathology. We hypothesize that *Ascaris* co-infection influences the efficacy of artemisinin-based combination treatment (ACT), *ex vivo* susceptibility, parasite clearance time, and reinfection rates, which might be attributable to variations in cytokines and antimalarial antibodies in *Ascaris* co-infection.

We will assess the named ACT efficacy outcomes among patients monitored according to WHO protocols. STH infection (miniFLOTAC) and anti-*Ascaris* antibodies (ELISA) will be determined. Antimalarial immunity at treatment initiation will be assessed by cytokine levels, monocyte-*P. falciparum* stimulation assays (cytokine read-out), and antimalarial antibodies and related to efficacy outcomes in addition to *Ascaris* co-infection. Children with recurring parasitaemia will be sampled and *P. falciparum* resistance markers typed.

https://tropeninstitut.charite.de/en/

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C8

Supervisor: Emanuel Heitlinger

Research Group: Molecular parasitology (HU)
Ecology and Evolution of parasite-host interactions (IZW)

Address: Department of Molecular Parasitology, Humboldt University,
Philippstr 13, Haus 14

Resistance and tolerance of hybrid hosts against co-infections -- the role of innate immune response and the microbiome for mice in natural systems

Natural hybrids between the house mouse subspecies show increased parasite resistance but also perturbed bacterial microbiomes compared to pure parental strains. Laboratory infections of Rag-/- mutant mice with *E. falciformis* revealed partial resistance to repeated infection independent of the adaptive immune system.

We here hypothesize, that 1) the innate immune system plays a key role in the immunological vigor of hybrid hosts, and that 2) this holds true for infections with *Eimeria*, helminths and for co-infections, while 3) a perturbed hybrid microbiome affects parasites negatively.

A collection of tissue and intestinal content samples of ~200 mice, spanning a continuous gradient of hybridization will be investigated for parasites and the intestinal microbiome via 18S and 16S amplicon sequencing. “Dual-transciptomes” assessing gene expression for both host (cecum tissue) and *Eimeria* sp. will be integrated with this and with immunological assessments from laboratory experiments.

https://www.biologie.hu-berlin.de/en/gruppenseiten-en/molpara-en/standardseite?set_language=en

http://www.izw-berlin.de/en/emanuel-heitlinger-en.html

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C9

Supervisor: Friederike Ebner

Research Group: Institute of Immunology

Address: Institute of Immunology, Freie Universität Berlin,
Robert-von-Ostertag-Str. 7-13, 14163 Berlin

The role of antigen-specific T cells in parasite distribution and predisposition to *Ascaris suum* in pigs

The large roundworms *Ascaris* (*A.*) *lumbricoides* and *A. suum* are the most prevalent soil-transmitted helminths (STH) worldwide and parasitize the gastrointestinal tract of humans and pigs, respectively. *A. suum* infections are economically relevant and highly prevalent in intensive and organic pig productions worldwide. We typically observe that only a few individuals harbor a very high number of worms, a phenomenon called overdispersion. The reasons for low and high worm burdens are unclear.

This project aims at investigating the role of highly specialized T cells to assess and control parasite burden in pigs as a human-relevant model. Benefitting from a recently established method to enrich and phenotype antigen-specific T cells in swine, the project will explore effector, memory and recall responses of A. suum-specific T cells and their role for parasite predisposition. Experimental infections with one or multiple inoculations will be performed and re-infection rates addressed.

The successful candidate will develop their skills in working with a human-relevant animal model, advanced flow cytometry, cell culture and parasitology.

https://www.vetmed.fu-berlin.de/en/einrichtungen/institute/we06/index.html