

Call for applications for

Two scholarships for doctoral projects in Parasitology, Berlin

Term: 3 years – start: 01.01.2021

Confirmatory sign: GRK2046 – ES

Working place: Berlin-Düppel (AG Hartmann / Ebner), Robert-von-Ostertag-Str. 7-13

Description Project 1

The intestine is a key organ for many chronic inflammatory diseases. Here, numerous functions of digestion, the regulation of the immune system and the microbiome are interconnected. The ubiquitous intestinal roundworm *Ascaris* spp. infects humans and livestock alike and belongs to the intestinal microbiome. While the immune system usually tolerates irrelevant stimuli ("immune tolerance"), in chronic inflammatory diseases such triggers lead to inflammation. In industrial and developing countries inflammatory bowel diseases (IBD: Crohn's disease, ulcerative colitis) are significantly on the rise. The incidence of these diseases is particularly high among young individuals (15 to 35 years). In parallel, *Ascaris* infections in humans and pigs are common in young individuals/pigs and childhood exposure to *Ascaris* may foster immune education and the appropriate instruction of immune tolerance.

Aim of the project is to understand how *Ascaris* and gut microbes synergize in promoting gut health, this project aims to **characterize the adaptive T cell responses to *Ascaris* and gut microbes in *Ascaris*-infected humans as well as pigs.**

The work program comprises:

- Human and gut porcine microbial signatures during *Ascaris* infection
- Number, phenotype and function of circulating blood CD4⁺ T cells reactive against *Ascaris* antigen (excretory/secretory products of larval and adult stages), prominent commensals / pathogens (e.g. *E. coli*, *Lactobacillus*, *Bifidobacteria*, *Bacteroides*, *Salmonella typhimurium*, *Clostridium difficile*)
 - in *Ascaris*-infected individuals versus endemic normal (peripheral blood)
 - in *Ascaris*-infected / naive pigs with and without induction of TNBS-induced colitis (peripheral blood and intestine)
 - IgA / IgE response against *Ascaris* and gut microbes
- Effect of microbial metabolites and *Ascaris* ES products on immune cells (regulatory dendritic cells and monocytes / macrophages) in humans and pigs
- Intestinal barrier integrity and defense program of intestinal epithelial and immune cells in healthy versus *Ascaris*-infected pigs: metabolic activity, mucus viscosity and NAD(P)H fluorescence lifetime imaging (FLIM) (cooperation with Raluca Niesner, Berlin)

References:

Midha A *et al.* 2020. Trilateral relationship: *Ascaris*, Microbiota and host cells. *Trends Parasitol*, doi: 10.1016/j.pt.2020.09.002.

Midha A *et al.* 2018. The intestinal roundworm *Ascaris suum* releases antimicrobial factors which interfere with bacterial growth and biofilm formation. *Front Cell Infect Microbiol*, doi: 10.3389/fcimb.2018.00271.

Hegazy AN *et al.* 2017. Circulating and tissue-resident CD4⁺ T cells with reactivity to intestinal microbiota are abundant in healthy individuals and function is altered during inflammation. *Gastroenterology*, 153:1320-37.

Description Project 2

Currently, the possible interactions between helminth infection and the outcome of viral pneumonia are intensively discussed (1,2). On the one hand, systemic immunomodulatory effects of helminths (e.g. IL-10 and T_{reg} induction, alternatively activated macrophages (AAMs)) and the type 2 (Th₂) skewed host immune response

capable to suppress type 1 immunity might moderate pulmonary inflammation. On the other hand, pulmonary pathology is associated with eosinophil infiltration and lung fibrosis mediated by perivascular infiltrating AAMs, both being hallmarks of the helminth-induced immune response.

For *Ascaris*, being one of the most common human intestinal parasites, this topic can be studied experimentally in pigs - the natural hosts for zoonotic *Ascaris suum*. Upon infection, *Ascaris* larvae start tissue migration through liver and lungs and induce acute lung pathology before establishing chronic infection in the gut. Hence this project will exploit the dual roles of *Ascaris* infection - acute larval lung injury and chronic, immunomodulatory intestinal infection - on the outcome of pneumonia.

Perspective for human medicine: Experimental pig infections allow us to study the tissue-specific but also systemic pathogen-specific T helper cell responses that orchestrate pathogen control and possibly indicate disease severity and parasite burden. This knowledge on blood-derived, pathogen-specific Th cell phenotyping can be applied and transferred to helminth-endemic regions.

References:

- Bradbury RS *et al.* 2020. Will helminth co-infection modulate COVID-19 severity in endemic regions? *Nat Rev Immunol*, 20:342.
- Hays R *et al.* 2020. Helminth coinfection and COVID-19: An alternate hypothesis. *PLoS Negl Trop Dis*, 14:e0008628.
- Schmidt S *et al.* 2020. The domestic pig as human-relevant large animal model to study adaptive antifungal immune responses against airborne *Aspergillus fumigatus*. *Eur J Immunol*, 10.1002/eji.201948524.
- Braun J *et al.* 2020. SARS-CoV-2-reactive T cells in healthy donors and patients with COVID-19. *Nature*, 587:270-4, doi: 10.1038/s41586-020-2598-9.
- Le Bert N *et al.* 2020. SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls. *Nature*, 584:457-62.

Expected:

- Master / Diploma or a similar university degree in a relevant subject (e.g. Staatsexamen Veterinärmedizin)
- Experiences in veterinary medicine or / and Parasitology (laboratory work)
- Good skills in English language (written and spoken)
- Basic Computer skills with MS office programs
- Interest in field work in Africa (1-3 month per year)

GRK2046:

You will be associated to the Research Training Group 2046, which gives you the opportunity to take part in many GRK-events with other PhD students. GRK 2046 may finance your travel to conferences and transferable skill courses. You have the chance to (co-)organize events, like workshops and retreats. In addition, you will profit from the educational program of our GRK.

Application:

We expect at minimum a complete *Curriculum Vitae* including all relevant certificates, two reference letters by two different referees and a letter of motivation (including why you want to work in Parasitology, why you want to work in these projects; future career plans). Send your application as **one PDF e-mail attachment via E-mail only** to grk2046@fu-berlin.de, subject: Application Einstein scholarships. Please note: incomplete applications cannot be considered

This call will close at 10.12.2020. Interviews will take place in Berlin or online before Christmas.