Doctoral student call

Project Title: Expression of *Plasmodium falciparum* variant surface antigens during dry season asymptomatic infections.

Project leader: Silvia Portugal  
Source of Funding: ERC

Application Deadline: March 31st  
Start of PhD project: June 2018

We are seeking an enthusiastic PhD student to join our laboratory at the Parasitology Department of Heidelberg University Hospital.

Project Description: We have recently shown that dry season *Plasmodium falciparum* infections are maintained asymptomatically during the 6-month dry season in Mali, while *P. falciparum*-specific humoral responses decrease (Portugal, S. et al. 2017).

During the latter part of the 48h erythrocytic cycle and in order to avoid clearance by the spleen, *P. falciparum* expresses one of its ~60 *P. falciparum* erythrocyte membrane protein 1 (PfEMP1), encoded by var genes, on the erythrocyte surface to promote cytoadherence to blood vessel endothelial cells (Storm, J. et al. 2014). Malaria immunity is partially mediated by acquiring IgG binding to, and inhibiting PfEMP1. This leads to an evolutionary arms race between the parasite itself and the host immune system. As the host responds to a given parasite antigen with antibody production, the parasite changes its expressed protein to avoid host clearance. In the case of PfEMP1, with each subsequent blood stage parasite generation a small fraction of progeny switch to express a different var gene, allowing evasion of IgG responses during the infection. var genes encoding PfEMP1 are highly diversified in sequence but conserved in domain structure and composition, and specific variants confer immunogenic and cytoadhesive phenotypes that may determine the clinical outcomes of infection (Lavstsen, T et al. 2012; Jespersen, JS et al. 2008; Kaestli, M et al. 2006; Kirchgatter, K. et al. 2002). However, no study has addressed the expression profile of PfEMP1 encoding var genes during the chronic phase of blood stage infection in the dry season, a time during which new *P. falciparum*-specific antibodies seem not to be produced.

Thus, we now aim to understand how expression variant surface antigens such as PfEMP1 are modulated during the 6-month dry season. Specifically, we will determine which type of PfEMP1 genes are expressed by parasites during the dry season and how effectively they are detected by the immune system. We will sequence the transcribed PfEMP1 genes of individuals carrying chronic and asymptomatic *P. falciparum* parasites at different time-points during the six-month dry season to establish if specific variants are selected during this time, and at which rate new variants emerge. We will also determine the dynamics of humoral responses to different PfEMP1s during the dry season. These results will reveal if certain PfEMP1 types or traits are associated with asymptomatic infection in the dry season, and how pressure from the immune system contributes to PfEMP1 variant switching.
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References:
*Storm J, Craig AG Pathogenesis of cerebral malaria--inflammation and cytoadherence* Front Cell Infect Microbiol 2014
*Kaestli M, Cockburn IA, Cortes A, Baea K, Rowe JA, Beck HP Virulence of malaria is associated with differential expression of Plasmodium falciparum var gene subgroups in a case-control study* J Infect Dis 2006
*Kirchgatter K, Portillo Hdel A Association of severe noncerebral Plasmodium falciparum malaria in Brazil with expressed PIEMP1 DBL1 alpha sequences lacking cysteine residues* Mol Med 2002

Methods to be used: RNA extraction, qRT-PCR, DNA and RNAsseq, bioinformatics, cell culture, molecular biology

Collaboration Partners: Peter Crompton (NAID, NIH), Boubacar Traore (FMPOS, ICER Mali), Thomas Lavstsen (Copenhagen University), Antoine Claessens (MRC The Gambia)

Profile of candidate's qualification:
- Graduate or Master’s Degree in Biology or related areas; work practice in *Plasmodium* infection is desirable; as well as experience/knowledge of cell culture, q-RT PCR, bioinformatics and statistics
- Excellent knowledge of spoken and written English and excellent communication skills and team spirit; organizational skills and ability to keep detailed records of experiments;
- Critical mind and enthusiasm;) and ability to work in multidisciplinary and multicultural teams.

Keywords: *Plasmodium falciparum*, malaria, dry season, var genes, PfEMP1

Contact: HBBIGS website, Project no: Portugal0118; apply here
Send one motivation letter and your CV along with two reference letters, until the 31st of March