Project description

Project Title: Immune Correlates of Protection against *Plasmodium berghei* Infections

Research Group: Molecular Parasitology
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Project Description:

The project aims at identification of immune signatures of protection and designing a multi-stage Genetically Attenuated Parasite (GAP) line for further preclinical research and potential translation to clinical trials.

Plasmodium parasites have a complex life cycle involving a mosquito and a vertebrate host. In the vertebrate host a sporozoite enters the host liver, transforms and forms merozoites, the so-called pre-erythrocytic development before initiation of the pathogenic blood stage infection. During liver infection a protective CD8 T cell-mediated immune response is initiated, whereas a blood infection induces antibody responses that can lead to semi-immunity. GAPs are *Plasmodium* parasite lines that are used as vaccines as they are attenuated in the host liver by genetic modifications and not able to initiate blood stage infections.

In the first part of this project, life attenuated, but non-invasive sporozoite lines will be tested in comparison to protective GAPs. Immune profiling of these vaccine cohorts will be done in spleens, livers, draining lymph nodes, and blood. For immune profiling, the student will quantify immune cells with a focus on the T cell repertoire and intracellular cytokine levels. We hope to identify distinct cells that are activated during protective immunizations, but not during sporozoite exposure with non-invasive parasites.

In the second part of this project, major antigens originating from *Plasmodium* blood stage merozoites, such as Merozoite Surface Protein 1 (MSP1) and Apical Membrane Antigen 1 (AMA1), will be used as starting points for experimental validation of the possibility to express merozoite proteins on the *Plasmodium* sporozoite surface. We hypothesize that this strategy leaves pre-erythrocytic immune responses unaffected but elicits additional blood stage-specific immune responses that are missing in immunizations with first generation GAPs. Upon a blood stage challenge, which is known to be unaffected by immunizations with first generation-GAPs, or a sporozoite challenge after low-dose immunizations, blood stage-specific B and T cell responses might provide partial protection against blood stage replication and disease and, hence, constitute an important improvement towards a multi-stage malaria vaccine strategy.