

**Title: Screening of compounds against malaria parasites**

**Synopsis:**

Malaria is caused by protozoan parasites of the genus *Plasmodium* and remains one of the most prevalent infectious diseases in the world, affecting primarily children under the age of 5 years old. Despite the achievements in the treatment of malaria, there is still an urgent need for the discovery of new drugs that tackle infection by *Plasmodium*. The initial step of infection of the mammalian host is clinically silent and takes place in the host's liver. This obligatory phase of hepatic infection is ensued by the symptomatic blood stage of infection. Thus, targeting these steps of parasite infection provides an opportunity for prophylaxis and treatment, respectively.

This Master's Thesis Proposal will focus on the *in vitro* screening of compounds for their potential activity against the liver and blood stages of infection by the rodent *P. berghei* and the human *P. falciparum* parasites, respectively. Initially, compounds will be screened for their overall activity against *P. berghei* liver stage by a well-established, bioluminescence-based, assay. Next, their activity will be further assessed by flow cytometry and fluorescence microscopy techniques to identify the specific steps of hepatic infection that are affected by the compound. Compounds will also be screened for their activity against *P. falciparum* blood stage by bioluminescence- and/or flow cytometry-based assays. When relevant, compounds may further be screened for *in vivo* insecticidal activity employing an artificial membrane feeding-based assay. Collectively, results obtained will inform the selection of hit compounds that may subsequently be tested *in vivo* in a rodent model of *Plasmodium* infection.

Overall, this project has the potential to identify new compounds that act against the liver and/or blood stages of *Plasmodium* infection, which can contribute to the global effort of malaria eradication.

**Supervisor:** Diana Fontinha, Miguel Prudêncio Lab, [dfontinha@medicina.ulisboa.pt](mailto:dfontinha@medicina.ulisboa.pt)

**Co-Supervisor:** Miguel Prudêncio, Miguel Prudêncio Lab, [mprudencio@medicina.ulisboa.pt](mailto:mprudencio@medicina.ulisboa.pt)

**Contact:** [dfontinha@medicina.ulisboa.pt](mailto:dfontinha@medicina.ulisboa.pt)

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**Bibliography:**

Prudencio, M.; Mota, M. M.; Mendes, A. M. (2011), "A toolbox to study liver stage malaria", *Trends in Parasitology*, 27 (12), 565-74.

Singh, L., D. Fontinha, D. Francisco, A. M. Mendes, M. Prudêncio, and K. Singh. (2020), "Molecular Design and Synthesis of Ivermectin Hybrids Targeting Hepatic and Erythrocytic Stages of Plasmodium Parasites.", *J Med Chem*, 63 (4):1750-1762.