Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: Drug repurposing against malaria parasites

Synopsis: Malaria is caused by protozoan parasites of the genus *Plasmodium* and it is still 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 obligatory and clinically silent nature of the liver stage of the *Plasmodium* life cycle in the mammalian host makes it an appealing target for drug development. However, this is a costly and time-consuming process. An alternative strategy is to identify compounds that are already approved for other purposes, which might display anti-plasmodial activity, an approach known as drug repositioning or repurposing.

This project will focus on the screening of compounds that are therapeutically relevant in the context of diseases that are prevalent in regions where malaria is endemic. Compounds will be tested *in vitro* for their potential activity against the hepatic stage of the rodent parasite *Plasmodium berghei*, as well as against the blood stage of the human malaria-causing parasite *P. falciparum*. Results obtained will possibly inform the selection of hit compounds to be tested *in vivo* in a rodent model of *Plasmodium* infection.

Furthermore, *in vitro* assays to assess liver stage activity are currently carried out in a 96-well plate format. In order to increase the compound number capacity and to improve the cost-effectiveness of the assay, this project will additionally involve the establishment of a screening protocol employing a 384-well plate format.

Overall, this project has the potential to identify a new purpose for pre-existent approved drugs, which can contribute to the global effort of malaria eradication.

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Bibliography:

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