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Abstract Proyecto Actual

Malaria is an infectious disease caused by plasmodium parasite transmitted by female Anopheles mosquitoes. There are five species of malaria that can infect humans: *P.vivax, P.malariae, P.ovale, P.falciparum and P.knowlesi.* Malaria is the leading cause of death in tropical countries. According to the 2016 WHO World Malaria Report, in that year, 216 million cases and 445,000 deaths were recorded. Children under the age of five from sub-Saharan Africa are the most affected. There is an urgent need to find new antimalarial drugs because of the increasing antimalarial drug resistance of the parasite and the increasing pesticides resistance of the vector. The ATP-binding casette (ABC) superfamily is a family of protein transporters that plays a role in detoxification and drug resistance. Eukaryotes have 8 subfamilies: ABCA, ABCB, ABCC, ABCD, ABCE, ABCF, ABCG and ABCH. Our laboratory has demonstrated that mutant *Plasmodium berghei* parasites without the *abcg* gene, which codes for ABCG transporters, show less susceptibility to the drugs chloroquine, artemisinin, artesunate and dihydroartemisinin. These mutants also have a higher expression of the genes *pbgst*, *pbtrx1* and *pbtrx2* which are involved in the glutathione and thioredoxin systems, the primary line of defense of the parasites against oxidative stress. We hypothesize that glutathione S-transferase (GST) plays a role in the antimalarial drug resistance in the *abcg*- parasites and increased number of gametocytes. Our first aim is to determine if GST plays a role in antimalarial drug resistance in the mutant *Plasmodium berghei* parasite. To do this, we will evaluate the susceptibility of *abcg*- mutant parasites to antimalarial drugs by *in vitro* drug essays in the presence of S-hexylglutathione, a specific GST inhibitor, and determine the EC50's of antimalarial drugs in *abcg*- and wild type parasites in the presence of S-hexylglutathione. Our second aim is to study the morphology of *Plasmodium* mutants during intra-erythrocytic development as compared to the wild type. This research will further our knowledge of parasite resistance to antimalarial drugs.