Plasmodium falciparum heme species dynamics under antimalarial exposure

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While the recently approved first malaria vaccine provides new hope with a reduction in deadly severe malaria, decreasing the disease burden towards elimination requires highly effective drug treatment. However, treatment efficacy is constantly challenged by the capacity of *Plasmodium falciparum* parasites to develop resistance. The present artemisinin-based combination therapy is no exception. As the portfolio of new drugs is limited, identifying new targets and developing new therapies to tackle malaria is urgent. Most antimalarial drugs somehow target the heme detoxification pathway, happening in the symptomatic intraerythrocytic developmental cycle (IDC) of parasite infection in the human host. During the IDC, parasites feed on hemoglobin, which is endocytosed to the digestive vacuole, originating free heme. Free heme is harmful to the parasite and, thus, it is converted into the inert hemozoin crystal. Herein, we explore a cell fractionation assay that allows to measure the parasite's heme species in complex with pyridine and measured the levels of specific heme fractions along tightly synchronized parasites' lifecycle in the presence of antimalarials. This approach led to characterize the dynamics of these heme species throughout the IDC, unveiling the stages where antimalarials most impact the heme species dynamic balance.