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# Role of Heme Detoxification Protein in *Plasmodium falciparum* Heme Metabolism

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The malaria parasite, *Plasmodium falciparum*, exports hundreds of proteins into its host erythrocyte, modifying it in many ways critical to the parasites survival and replication. Of the many modifications made to the host erythrocyte, the degradation of hemoglobin and the metabolism of heme is crucial to the biology of the malaria parasite. During its intraerythrocytic stages, the parasite sequesters heme from hemoglobin into hemozoin crystals stored in a lysosome-like compartment called the food vacuole to prevent free heme toxicity. Jani et al. identified a novel parasite protein potent in converting free heme into hemozoin, which they termed Heme Detoxification Protein (HDP). Using Cas9 guide RNA's known to successfully target the locus, we were unable to disrupt the locus and insert a drug selection cassette to create an HDP knockout line, supporting evidence that HDP is essential to parasite intraerythrocytic stages. Using a CRISPR/Cas9 introduced regulatable aptamer knockdown system to inhibit translation of HDP mRNA, we have found that parasites in the knockdown condition are unable to survive. However, there is a significant delay in observing this, suggesting that HDP has a low turnover rate, and is passed on to daughter parasites. Using these lines, we are currently performing hemozoin quantification experiments, allowing us to quantify the effects of HDP knockdown on parasite hemozoin levels.

HDP does not contain a protein export element (PEXEL) signal sequence, a motif frequently found on *Plasmodium* proteins that are transported out of the parasitophorous vacuole. Jani et al. described a circuitous trafficking pathway taken by HDP, however, the evidence was not strong in supporting this conclusion. By tagging HDP with a Neon Green tag in HSP101 export regulatable parasite lines, we hope to also elucidate HDP's trafficking pathway via live microscopy.