The biological interrogation of *Plasmodium falciparum's* putative mitochondrial pyruvate carrier

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Introduction: *Plasmodium falciparum,* the most clinically important malaria-causing parasite, continues to impose a socio- economic burden on the African population. Scientific efforts are targeted towards malaria eradication through identification of novel chemotherapeutics and further interrogation of parasite biology. *P. falciparum* uses components of energy metabolism in a unique manner from one intraerythrocytic form to the next. The proliferative asexual stage fulfils its rapid energy demand through anaerobic glycolysis. However, the metabolically quiescent gametocyte, the transmissible form, relies on the canonical TCA cycle. Pyruvate production is important for both stages, yet its translocation across the mitochondrial membrane is fundamental to driving the gametocyte TCA cycle. In the last decade, the mitochondrial pyruvate carrier (MPC) responsible for pyruvate translocation in humans, yeast and *Drosophila* was identified. In *P. falciparum, mpc* genes have been putatively annotated but are not yet characterised.

Methodology: In this study, the biological importance of the putative MPC to the parasite was investigated through chemical interference with a known MPC inhibitor and genetically manipulated using a targeted disruption tool.

Result and discussion: The MPC inhibitor displayed growth and viability inhibitory activity (IC_{50}) against *P. falciparum* in the micromolar range. Moreover, chemical inhibition induced a slight delay in morphological stage progression. The genetic disruption of individual *mpc* genes indicated *mpc1* to be essential to asexual parasite survival, whereas *mpc2* is dispensable. This challenges the thought of the sole importance of pyruvate translocation to gametocytes and further investigations are needed to expand on the intricacies surrounding pyruvate transport.

Keywords: Malaria, parasite, energy metabolism, Mitochondria, Pyruvate, Carrier