SOCIÉTÉ CHIMIQUE DE GENÈVE

Plasmepsin IX and X: new candidate targets for old antimalarial drugs

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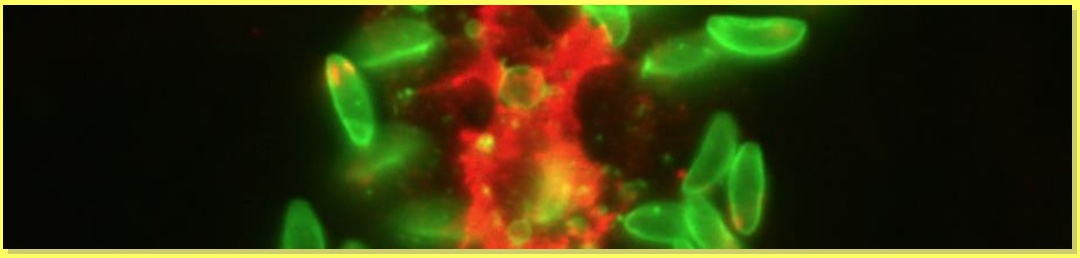
Host cell entry and egress from infected cells are key events in the lytic cycle and dissemination of Apicomplexan parasites. The rearward translocation of apically secreted adhesins propels the parasite inside the host cell and involves a connector that physically links the adhesins to the parasite actomyosin system. In *Toxoplasma gondii*, ASP3 is an essential aspartyl protease that plays a central role in invasion and egress by acting as maturase on a series of key adhesins. ASP3 clusters phylogenically with two aspartyl proteases in *Plasmodium falciparum,* the Plasmepsins IX and X. Importantly a highly potent antimalarial compound originally directed against the Plasmepsins implicated in haemoglobin degradation, selectively blocks egress of malaria parasite from red blood cells at subnanomolar concentration. We hypothesise that this compound selectively inhibits Plasmepsin IX and X that are essential for parasite propagation and hence potential target for intervention.



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