Australian National University

PUBLIC LECTURE

PhD Exit Seminars

Xie Wah Audrey Chan & Nimeka Ramanayake

Friday 25 October 2013 4pm

Slatyer Seminar Room Building no. 46, Linnaeus Rd, ANU

Thiamine utilisation by the malaria parasite *P. falciparum*
Xie Wah Audrey Chan, Saliba lab, BSB

The parasite's thiamine (vitamin B1) biosynthesis capacity is insufficient to meet its requirements, and the parasite, therefore, needs to scavenge extracellular thiamine. Thiamine utilisation by the *P. falciparum* parasite might therefore serve as a potential antimalarial drug target. The mechanism of thiamine transport and its accumulation in the *P. falciparum* parasite was investigated in some detail. So too was the antiplasmodial activity of various thiamine analogues. This study found that oxythiamine inhibited *in vitro* parasite proliferation via a thiamine-related pathway. Oxythiamine has been shown to significantly inhibit parasite proliferation in a mouse model of malaria, providing evidence that the parasite's thiamine utilisation pathway is a viable antimalarial drug target. The antiplasmodial mode of action of oxythiamine was investigated by targeted overexpression of key enzymes in thiamine metabolism and utilisation. Data will be presented on these parasite lines' sensitivity to the thiamine analogues and capacity to accumulate thiamine.

Vacuolar-type H^+-pumping pyrophosphatases in *P. falciparum*
Nimeka Ramanayake, Saliba Lab, BSB

Vacuolar-type H^+-pumping pyrophosphatases (V-H^+-PPases) are primary active transporters that utilise the energy from PP_i hydrolysis to translocate H^+ ions across a biological membrane. The identification of this protein class in several disease-causing parasites, and its absence in human cells, has exciting implications for its potential as an antiparasitic drug target. The *P. falciparum* genome encodes putative K^+-sensitive (*PfVP1*) and K+-independent (*PfVP2*) V-H^+-PPases, and previous research has indicated the presence of V-H^+-PPase activity in the malaria parasite. In my research I focused on further characterization of this activity, in particular establishing a link between *PfVP2* gene expression and enzyme activity. I also investigated the impact of *PfVP2* gene deletion on parasite growth and drug sensitivity. Furthermore, I investigated the subcellular localisation of PfVP2 within the intraerythrocytic-stage malaria parasite using fluorescent-reporter protein techniques. My talk will focus on the PfVP2 localisation aspect of my work.

Presented by

Research School of Biology

ANU College of Medicine, Biology & Environment

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