Title:

Rodent and non-rodent malaria parasites differ in their phospholipid metabolic pathways

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Running title:

Phospholipid biosynthesis pathways in the *Plasmodium* genus

Abstract

Malaria, a disease affecting humans and other animals, is caused by a protist of the genus *Plasmodium*. At the intraerythrocytic stage, the parasite synthesizes a high amount of phospholipids through a bewildering number of pathways. In the human *Plasmodium falciparum* species, a plant-like pathway that relies on serine decarboxylase and phosphoethanolamine N-methyltransferase activities diverts host serine to provide additional phosphatidylcholine and phosphatidylethanolamine to the parasite. This feature of parasitic dependence towards its host was investigated in other *Plasmodium* species. *In silico* analyses led to the identification of phosphoethanolamine N-methyltransferase gene orthologues in primate and bird parasite genomes. However, the gene was not detected in the rodent *P. berghei*, *P. yoelii* and *P. chabaudi* species. Biochemical experiments with labelled choline, ethanolamine and serine showed marked differences in biosynthetic pathways when comparing rodent *P. berghei* and *P. vinckei*, and human *P. falciparum* species. Notably in both rodent parasites, ethanolamine and serine were not significantly incorporated into phosphatidylcholine, indicating the absence of phosphoethanolamine N-methyltransferase activity. To our knowledge, this is the first study to highlight a crucial difference in phospholipid metabolism between *Plasmodium* species. The findings should facilitate efforts to develop more rational approaches to identify and evaluate new targets for anti-malarial therapy.

Key words:

Plasmodium falciparum, *Plasmodium berghei*, *Plasmodium vinckei*, lipid, phospholipid biosynthesis, phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphoethanolamine N-methyltransferase, serine decarboxylase