VALIDATION OF THE VITAMIN B1 AND B6 BIOSYNTHESES AS POTENTIAL DRUG TARGETS IN MALARIA

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Vitamin B6 and B1 are cofactors of essential enzymes that are ubiquitous in all organisms. The biosyntheses of these cofactors have been analysed in fungi, bacteria and plants, whereas humans and other mammals depend entirely on the uptake of these vitamins via their diet. Recently it was shown that the human malaria parasite possesses enzymes for the synthesis of the active B6 vitamer, pyridoxal phosphate (PLP). The activity of the enzymes responsible for the B6 biosynthesis, Pdx1 and Pdx2, was found to be functional only in the presence of both proteins, indicating protein-protein interaction. Interestingly, in yeast vitamin B6 is a precursor of the vitamin B1 biosynthesis leading to the active cofactor thiamine pyrophosphate (TPP). The enzymes of a TPP biosynthesis are also present in the human malaria parasite and have been biochemically characterised, however, a linkage of both pathways via the pyrimidine branch is not present in *P. falciparum*, implying that both vitamin pathways act independently from each other. The occurrence of the vitamin B1 and B6 *de novo* synthesis pathways displays a potential new drug target, which can be exploited for the development of new chemotherapeutics against the human malaria parasite.