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Effect of Farnesyltransferase Inhibitor R115777 on Mitochondria of *Plasmodium falciparum*

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Abstract:

The parasite *Plasmodium falciparum* causes severe malaria and is the most dangerous to humans. However, it exhibits resistance to their drugs. Farnesyltransferase has been identified in pathogenic protozoa of the genera *Plasmodium* and the target of farnesyltransferase includes Ras family. Therefore, the inhibitor of farnesyltransferase has been suggested as a new strategy for the treatment of malaria. However, the exact functional mechanism of this agent is still unknown. In addition, the effect of farnesyltransferase inhibitor (FTIs) on mitochondrial level of malaria parasites is not fully understood. In this study, therefore, the effect of a FTI R115777 on the function of mitochondria of *P. falciparum* was investigated experimentally. As a result, FTI R115777 was found to suppress the infection rate of malaria parasites under *in vitro* condition. It also reduces the copy number of mtDNA-encoded cytochrome c oxidase III. In addition, the mitochondrial membrane potential ($\Delta\Psi m$) and the green fluorescence intensity of MitoTracker were decreased by FTI R115777. Chloroquine and atovaquone were measured by the mtDNA copy number as mitochondrial non-specific or specific inhibitor, respectively. Chloroquine did not affect the copy number of mtDNA-encoded cytochrome c oxidase III, while atovaquone induced to change the mtDNA copy number. These results suggest that FTI R115777 has strong influence on the mitochondrial function of *P. falciparum*. It may have therapeutic potential for malaria by targeting the mitochondria of parasites.

Keywords: Plasmodium falciparum, malaria, mtDNA, farnesyltransferase inhibitor, mitochondria