Title: Simulating the Efflux Models of Chloroquine in the Plasmodium Falciparum Resistance (PfCRT) Mechanism.

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Date: 2011

Abstract: Chloroquine (CQ), cheap and long history antimalaria has failed in the treatment of malaria. This work sought to simulate the CQ efflux models of the resistance mechanism(s) of the human malaria parasite, Pf to CQ in the acidic food vacuole of the parasite. Following the introduction of Chloroquine as a first-line antimalaria and most widely used drug for the treatment of malaria, it is also able to reduce the parasite load in people with a high level of immunity to the parasite and thus, cannot be out rightly replaced or abandoned because it now frequently fails owing to widespread resistance. We used the unique biochemical pathway of Pf(Plasmocyc ver. 11.6,2007), which CQ targets to deduce the resistance mechanism(s) deployed by pf during the active efflux process(net movement of chloroquine out of a cell in a direction opposite to that of the prevailing electrochemical gradient). The two efflux models are (i) Channel model enables protonated CQ to leak out of the food vacuole down its electrochemical gradient and (ii) Transporter model is an active efflux transport system extruding CQ from the food vacuole. Netlogo software tool was used in simulating the two models, the result revealed there is more rapid efflux of Chloroquine in the food vacuole which suggests that CQR parasites have an enhanced permeation pathway for CQ across the food vacuolar membrane. The method shows how resistance occurs during the efflux process and the important mechanisms P.f deplores for resisting CQ. Thus, dual drivers for malaria treatment and control.