Thesis Title	Studies on Adenylate Translocase of the Human Malaria Parasite, *Plasmodium falciparum* and Energy Requirement for Chloroquine Action
Name	Nantarudee Juabsamai
Degree	Master of Science (Biochemistry)
Thesis Supervisory Committee	Prapon Wilairat, Ph.D. Sakol Panyim, Ph.D.
Date of Graduation	15 May B.E. 2536 (1993)

ABSTRACT

To determine whether the AdT gene is amplified in chloroquine (CQ)-resistant isolates, and in order to determine the chromosomal location of the *P. falciparum* AdT gene, the parasite chromosomes were fractionated by FIGE. The *P. falciparum* genome was resolved into at least 10 chromosomes. The chromosome fractionation of ten different clones and isolates of *P. falciparum* revealed that there is considerable variation in chromosome size from one parasite clone/ isolate to another. The AdT gene was found to be located on a chromosome larger than chromosome 8 (probably chromosome 9). Gene probing of HindIII-digested DNA from CQ-sensitive and resistant *P. falciparum* isolates showed a single band with minor variation in band intensities which did not correlate with CQ resistance.

To determine the role of exogenous ATP on parasite growth and development, atractyloside (ATR), an AdT inhibitor, was used. Parasites grown within resealed red cells containing ATR were observed for 72 h and the results showed that ATR had no effect on

parasite development and growth, and had little effect on CQ sensitivity of the resistant parasites.

Mitochondrial (thenoyltrifluoroacetone [TTF], oligomycin, carbonylcyanide n-chlorophenyl hydrazone [CCCP], and 2,4-dinitrophenol [DNP]) and glycolytic (iodoacetamide) inhibitors were tested in combination with CQ to see the effect of ATP depletion on CQ sensitivity of both CQ-sensitive and CQ-resistant parasites. It was found that there is no difference in the sensitivities of CQ-sensitive and CQ-resistant parasites towards each of the drugs tested. CQ-sensitive parasite ($Tm4C_{8-2}$) showed an antagonistic interaction between CQ and all the inhibitors tested. CQ-resistant parasite (K1) exhibited a more complicated curve for all the inhibitors tested (synergistic at low concentration and antagonistic at higher concentration) except for CCCP which was synergistic at all concentrations.