

**CONSTRUCTION OF RANDOM MUTANT LIBRARY OF *Plasmodium*
falciparum DIHYDROFOLATE REDUCTASE AND ITS USE FOR
STUDY OF EVOLUTION OF ANTIFOLATE RESISTANCE
IN *Plasmodium berghei* MODEL**

WACHIRAPORN TIPSUWAN

**DOCTOR OF PHILOSOPHY
IN BIOCHEMISTRY**

**THE GRADUATE SCHOOL
CHIANG MAI UNIVERSITY
JANUARY 2012**

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

**CONSTRUCTION OF RANDOM MUTANT LIBRARY OF *Plasmodium*
falciparum DIHYDROFOLATE REDUCTASE AND ITS USE FOR
STUDY OF EVOLUTION OF ANTIFOLATE RESISTANCE
IN *Plasmodium berghei* MODEL**

WACHIRAPORN TIPSUWAN

**A THESIS SUBMITTED TO THE GRADUATE SCHOOL IN
PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY
IN BIOCHEMISTRY**

**THE GRADUATE SCHOOL
CHIANG MAI UNIVERSITY
JANUARY 2012**

CONSTRUCTION OF RANDOM MUTANT LIBRARY OF *Plasmodium falciparum* DIHYDROFOLATE REDUCTASE AND ITS USE FOR STUDY OF EVOLUTION OF ANTIFOLATE RESISTANCE IN *Plasmodium berghei* MODEL

WACHIRAPORN TIPSUWAN

THIS THESIS HAS BEEN APPROVED
TO BE A PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY
IN BIOCHEMISTRY

EXAMINING COMMITTEE

Somdet Srichairatanakool CHAIRPERSON

Assoc. Prof. Dr. Somdet Srichairatanakool

Chakrit Hirunpetcharat MEMBER

Assoc. Prof. Dr. Chakrit Hirunpetcharat

Ratana Banjerdpongchai MEMBER
Assoc. Prof. Dr. Ratana Banjerdpongchai

Chairat Uthaipibull MEMBER
Dr. Chairat Uthaipibull

S. Kamchonwongpaisan MEMBER
Dr. Sumalee Kamchonwongpaisan

THESIS ADVISORY COMMITTEE

Somdet Srichairatanakool ADVISOR

Assoc. Prof. Dr. Somdet Srichairatanakool

Chairat Uthaipibull CO-ADVISOR
Dr. Chairat Uthaipibull

S. Kamchonwongpaisan CO-ADVISOR
Dr. Sumalee Kamchonwongpaisan

10 January 2012

ACKNOWLEDGEMENT

Firstly, I wish to express my sincere gratitude and deepest appreciation to my major advisor, Assoc. Prof. Dr. Somdet Srichairatanakool for his valuable advices, excellent guidance and support throughout the course of my study.

I would like to thank to my co-advisors Dr. Chairat Uthaipibull, Dr. Sumalee Kamchonwongpaisan and Professor Yongyuth Yuthavong who always gave kind expert guidance, continuous encouragement and allowed me a chance to learn an advanced technology in *P. berghei* transfection at Protein-Ligand Engineering and Molecular Biology Laboratory, National Center for Genetic Engineering and Biotechnology (BIOTEC).

My special thanks are extended to all members of Protein-Ligand Engineering and Molecular Biology Laboratory at BIOTEC, for providing research techniques, friendship and entertainment during my thesis research time at BIOTEC. I also gratefully thank all staffs of Biochemistry Department for supporting during my study.

I am indebted to Thailand Graduate Institute of Science and Technology (TGIST), National Science and Technology Development Agency (NSTDA) for financial support and thank Medical Faculty Endowment Fund for partial support.

Finally, thanks must go to all member of my family for love and inspiration throughout my life.

Wachiraporn Tipsuwan