THE INTERFERENCE OF HUMAN IMMUNODEFICIENCY

VIRUS ASSEMBLY AND MATURATION BY

ANKYRIN REPEAT PROTEINS

SAWITREE NANGOLA

DOCTOR OF PHILOSOPHY

IN BIOMEDICAL SCIENCE

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่ Copyright[©] by Chiang Mai University All rights reserved

THE GRADUATE SCHOOL

CHIANG MAI UNIVERSITY

FEBRUARY 2011

THE INTERFERENCE OF HUMAN IMMUNODEFICIENCY

VIRUS ASSEMBLY AND MATURATION BY

ANKYRIN REPEAT PROTEINS

SAWITREE NANGOLA

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

THE GRADUATE SCHOOL

CHIANG MAI UNIVERSITY

FEBRUARY 2011

THESIS UNDER THE CO-DIRECTED THESIS CONVENTION BETWEEN CHIANG MAI UNIVERSITY AND UNIVERSITY OF PARIS XI

THE INTERFERENCE OF HUMAN IMMUNODEFICIENCY VIRUS ASSEMBLY AND MATURATION BY ANKYRIN REPEAT PROTEINS

SAWITREE NANGOLA

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

EXAMINING COMMITTEE

Mitshin Organiad Z MEMBER

Assoc. Prof. Chatchai Tayapiwatana, Ph.D.

MEMBER

Prof. Philippe Minard, Ph.D.

.....MEMBER

Prof. Pierre Boulanger, M.D.

and kenter i MEMBER

Prof. Watchara Kasinrerk, Ph.D.

Dr. Nicole Ngo-Giang-Huong, Ph.D.

28 January 2011

© Copyright by Chiang Mai University and University of Paris XI

ACKNOWLEDGEMENTS

This thesis is the whole story of my long journey in the PhD study to obtain a double degree from Chiang Mai University (Thailand) and University of Paris XI (France). During my long road to success, a great number of people became involved; thereby enriching my journey with their wisdom, encouragement, and assistance, often times extending care to me as if I were a member of their family. It is a pleasure to express my gratitude to all of them in this acknowledgement.

I would like to express my deepest gratitude and sincere appreciation to my thesis advisor, Assoc. Prof. Dr. Chatchai Tayapiwatana, for giving me the opportunity to be a Ph.D student in his laboratory. It was not only a place to gain infinite knowledge but his lab also became my second home. He gave me the confidence, excellent guidance, valuable suggestions and many encouragements throughout this study and for the revision of this thesis and manuscripts. His deep knowledge and logical way of thinking are a great value for me in proving every significant experiment and generating important ideas. Moreover, he also afforded me many valuable experiences and wise counsel that supported my maturation.

I am extremely grateful to my co-advisor, Prof. Dr. Philippe Minard for his help in providing me with excellent guidance, constructive suggestions and comments, and kind support throughout my study, and revision of my manuscripts. I would also thank you for leading me into the protein engineering world and bringing me to work in Laboratoire de Modélisation et d'Ingénierie des Protéines, Institut de Biochimie Moléculaire et Cellulaire (IBBMC), Université de Paris-XI, which became

iii

my third home. The door of his office was always open for me to discuss many topics, aiding not only my work for my thesis but also my life in France.

A part of my thesis work was performed at Laboratoire de Rétrovirologie & Pathologie Comparée, Université Claude Bernard Lyon I & INRA UMR-754. My grateful thanks to Prof. Dr. Pierre Boulanger and Dr. Saw-See Hong for their supervision, excellent suggestions, comments, encouragement, kind help, and warm welcome. I would also like to thank them for providing me with the chance to gain knowledge in baculovirus expression system in their lab in Lyon, which became my fourth home. I could not resist having visiting them in Lyon whenever I traveled back to France. I'm sincerely thankful also for Mlle Gaëlle Gonzalez and everybody in this laboratory for their warm friendship and kind help during working in Lyon.

I additionally need to express my gratitude to Prof. Dr. Watchara Kasinrerk for his valuable suggestions, kind help in the production of monoclonal antibody, and providing equipment throughout my thesis. I would like to thank Ms Napaporn Apiratmetheekun and Ms Witida Laopajon for their kind help in monoclonal production. I would also like to thank members in this laboratory for their friendship, kindness, and contributions for technical training in monoclonal production technique.

I would like to acknowledge and sincerely thank the following special people: Assist. Prof. Dr. Khajornsak Tragoolpua for his suggestions and kind assistance; Ms Usa Homnium and Mr. Sompot Saoin, my closest friends, for their warm and cheerful friendship; all of my sisters and brothers in the lab - Ms Kunthida Kitidee, Ms Tanatporn Chunkeson, Ms Weeraya Thongkham, Ms Wannisa Khamaikawin, Ms Supattra Suwanpairod, Mr Warachai Praditwongwan, Mr Supachai Sakkhachornphop, Mr Chairat Tunghiran, Mr Tawee Donchai - and all the staff in Assoc. Prof. Dr. Chatchai's Lab for their smiles, very warm friendship, kind help and all that they did to greatly encourage me and help me to persevere.

I would also like to express my gratitude to all the staff in the MIP lab, Dr. Michel Desmadril, Dr. Agathe Urvoas, Dr.Marie Valerio-Lepiniec, and Dr. Magali Aumont-Nicaise, Dr. Antione Dravelle for their kind help, suggestions, encouragement, very warm welcome and friendship, and contributions for technical training throughout my work. Thank you to Madame Stephanie for her help in documents and Madame Pierrette for her help in preparing equipment used in the lab and her delicious cakes. I express my great thanks to Mlle Asma Guelluz, my lovely Tunisian friend, for her warm friendship, and kind help during my work in the lab. I also want to extend thanks to friends in IBBMC for their friendship.

I am also indebted to Assistant Professor Dr. Wasana Sirirungsri, Faculty of Associated medical Sciences, Chiang Mai University, for her help to obtain the financial support from the Franco-Thai Collaboration Program.

My grateful thanks to Associate Professor Dr. Nopporn Sittisombut, Faculty of Medicine, Chiang Mai University, for his kind help to acquire many high quality pictures from Fluorescence Microscopy.

I am grateful to all personnel and faculty members for their assistance in using various instruments at the Department of Medical Technology and Biomedical Technology Research Center, Faculty of Associated Medical Sciences, Chiang Mai University. I would like to especially thank Khun Kongkham Kruawan who gave me special meals for lunch every day, Khun Tuanjai Ponsung for her kind help to prepare official documents and services, and Mr. Wisud Chaiwansin for his kind help.

This work was supported by a scholarship from *CHE*-PhD-THA scholarship from the Commission on Higher Education, Ministry of Education, Thailand, the Franco-Thai collaboration program. I would also like to express my gratefulness for all the grants from the Thailand Research Fund, the Research Chair Grant of National Sciences and Technology Development Agency (Thailand), National Science and Technology Development Agency (NSTDA), and i+Med Laboratories (iMED). Some parts of my thesis work was supported by Prof. Dr. Philippe's grant and Prof. Dr. Pierre's grant.

I would like to thank everybody who was important to the successful realization of thesis, as well as to express my apology that I could not mention every individual by name.

Finally, I deeply thank to my parent, Mr Boonrat and Madam Tassanee Nangola, my brother, Mr Permphoon Nangola and my lovely niece, N'Prin, for their constant love, encouragement, and support of all of my decisions and ideas, moreover, for giving me freedom of thought.

Copyright[©] by Chiang Mai University All rights rese^{Sawitree Nangola}