

The background of the slide is a microscopic image showing various cells and particles. There are several large, irregularly shaped cells with a granular or fibrous internal structure, colored in shades of purple, blue, and yellow. Some cells appear to be interacting or releasing small, white, circular particles. The overall scene is set against a light blue, slightly blurred background, suggesting a biological or medical context.

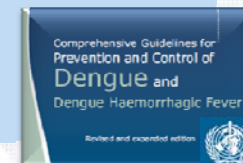
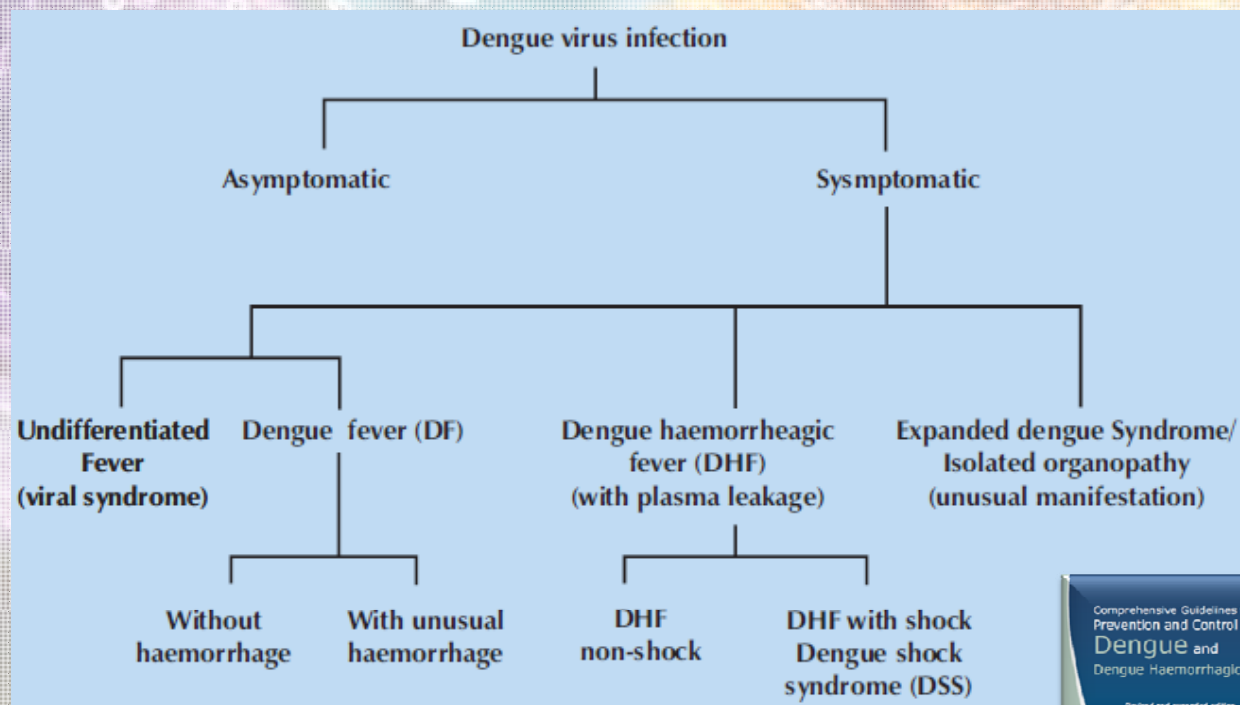
The role of cytokines and prediction of dengue complications

Hisham Imad MD, DTM&H, MCTM, CTH™

12th December 2018

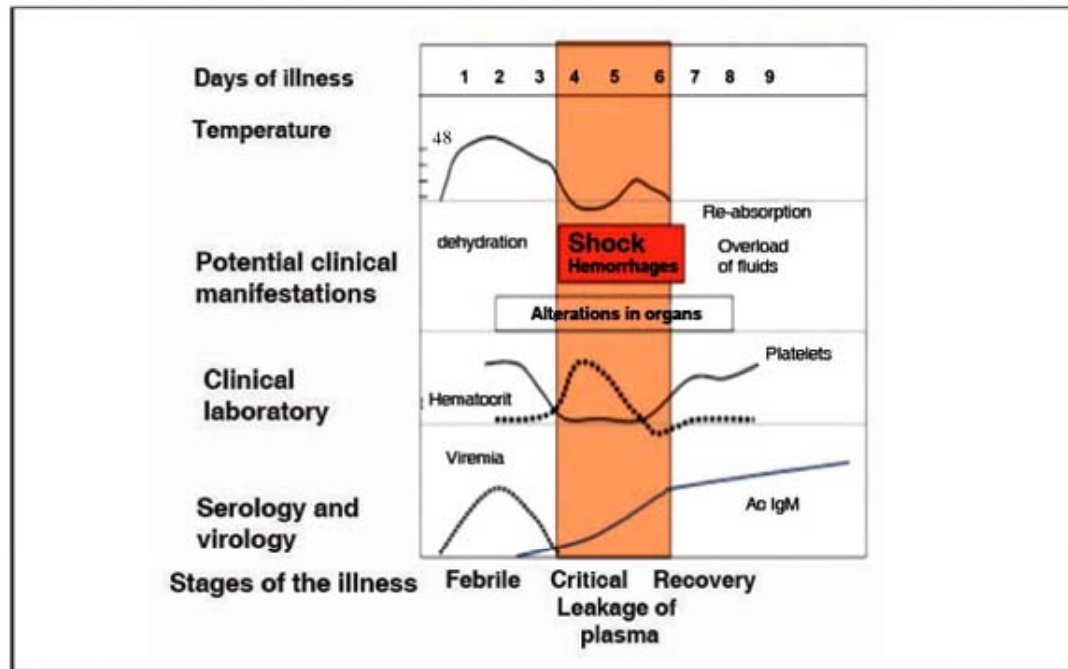
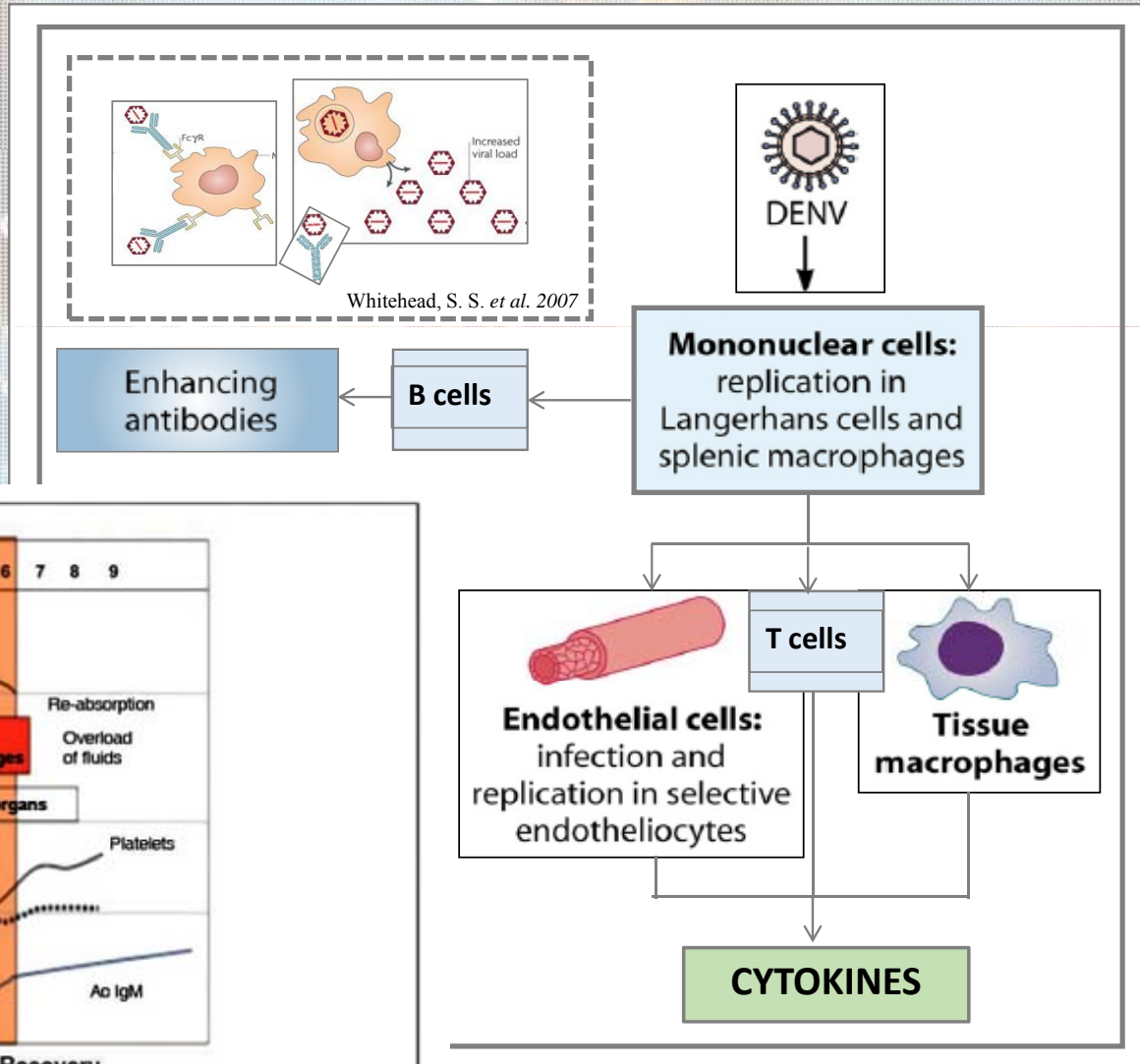
Introduction

- Dengue is the most common mosquito-borne *flaviviral* infection in the world today
- Several factors undoubtedly contribute to the developing of dengue complications



Pathogenesis

The plasma leakage mediated by the expressed cytokines causes endothelial dysfunction, increasing vascular permeability and bleeding.



Source: Formulated by Eric M. Torres.

Materials and Methods

Recruitment period – November 2015 – December 2016

Study site – Hospital for Tropical Diseases, Bangkok, Thailand

Subjects – Adults hospitalized with dengue infection

Inclusion:

- Age \geq 18 years
- Fever for a duration \leq 5 days
- Confirmation of dengue infection by
 - NS1 Ag positive
 - Anti DENV IgM positive

Exclusion:

- Vulnerable subjects
- Subjects who received any blood products during investigatory period

Cytokine measurements

Bio-Plex Human Cytokine Assay :IL-4, IL-6, IL-8, IL-10, IFN γ , TNF α (Bio-Rad Inc., Hercules)

Antibody assays

Commercially available Dengue IgM and IgG capture ELISA kits (Panbio Dengue Duo Cassette)

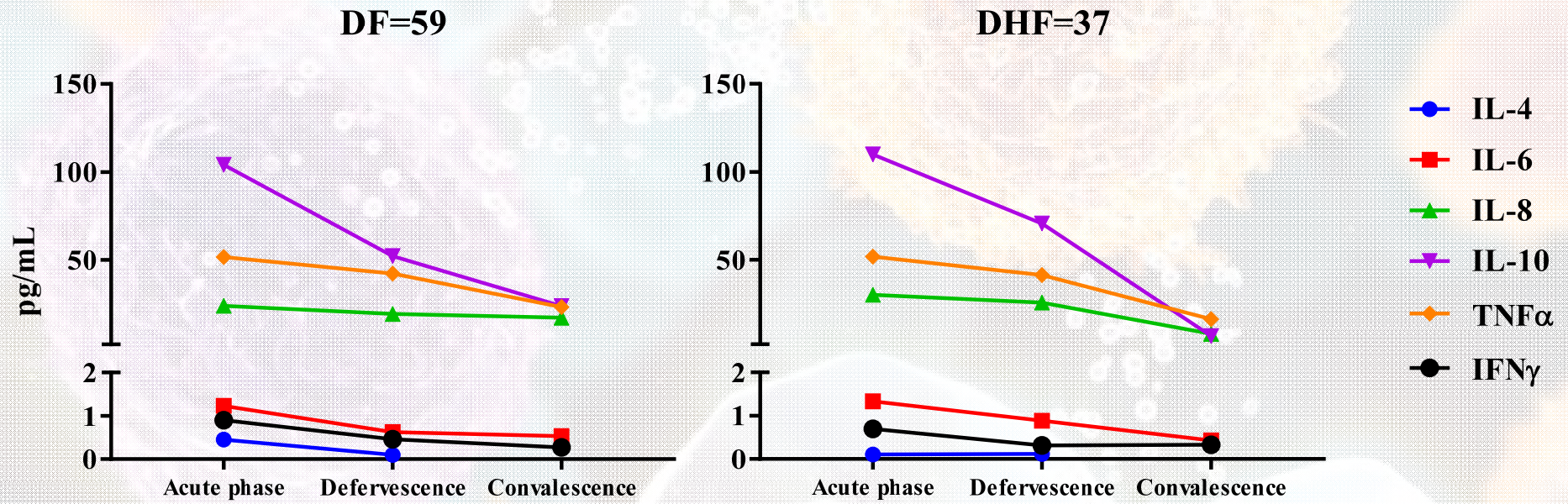
Serotyping

Dengue subtyping multiplex kit (Genesig Company)

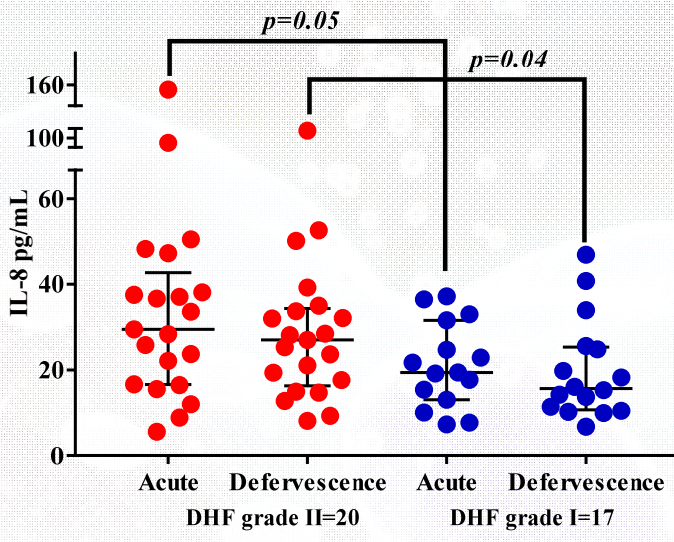
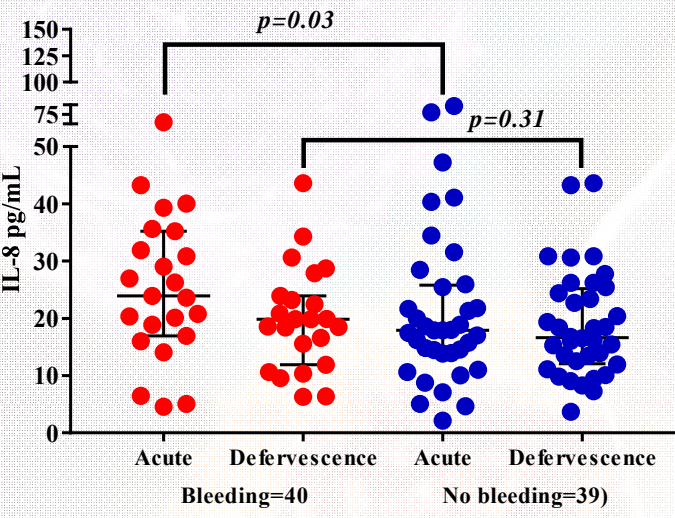
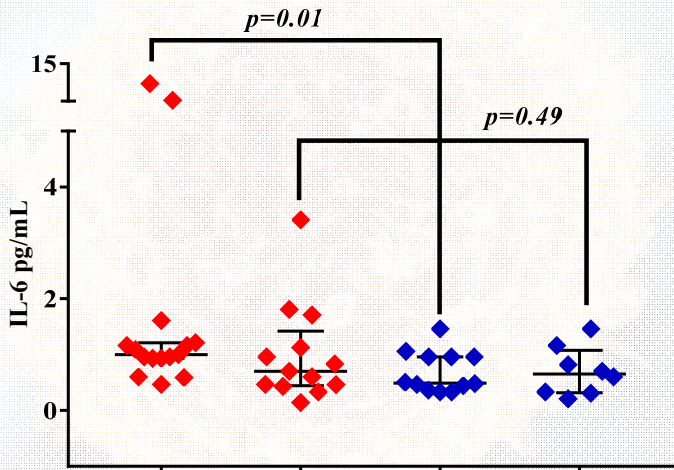
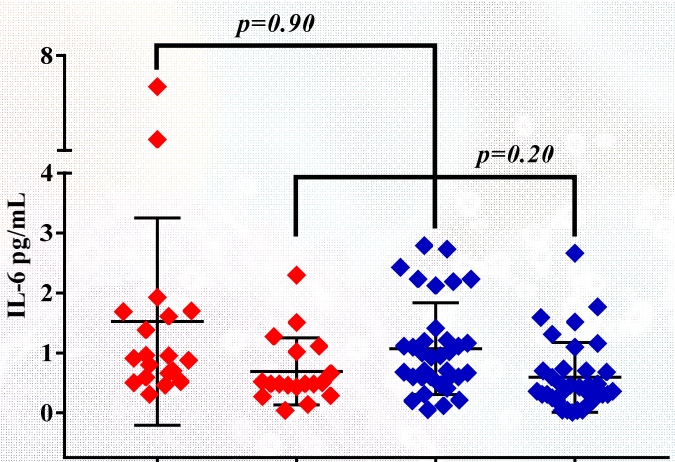
Clinical characteristics of DF vs. DHF

	DF = 61	DHF = 37	p value
	n (%)	n (%)	
Females	21 (34.42)	18 (48.64)	0.2
Males	40 (65.57)	19 (51.35)	
Age, mean±SD	31±11	33±11	0.44
Primary infection, age mean±SD	25±11	0	NA
Secondary infection, age mean±SD	32±11	33±11	0.11
Duration of illness, mean±SD	6.95±0.9	7.8±0.8	0.01
Fever	61 (62.24)	37 (37.7)	NA
Headache	53 (54.08)	37 (37.6)	0.02
Retro-orbital pain	26 (26.53)	22 (22.45)	0.1
Myalgia/Arthralgia	45 (45.92)	34 (34.69)	0.03
Loss of appetite	54 (55.10)	30 (30.61)	0.30
Nausea/Vomiting	31 (31.63)	20 (20.41)	0.75
Diarrhea	16 (16.33)	13 (13.27)	0.34
Lymphadenopathy	22 (36.07)	22 (59.46)	0.02
Hepatomegaly	18 (29.50)	15 (40.50)	0.31
Bleeding	20 (32.78)	20 (54.05)	0.05
Rash	30 (30.61)	19 (19.39)	0.83

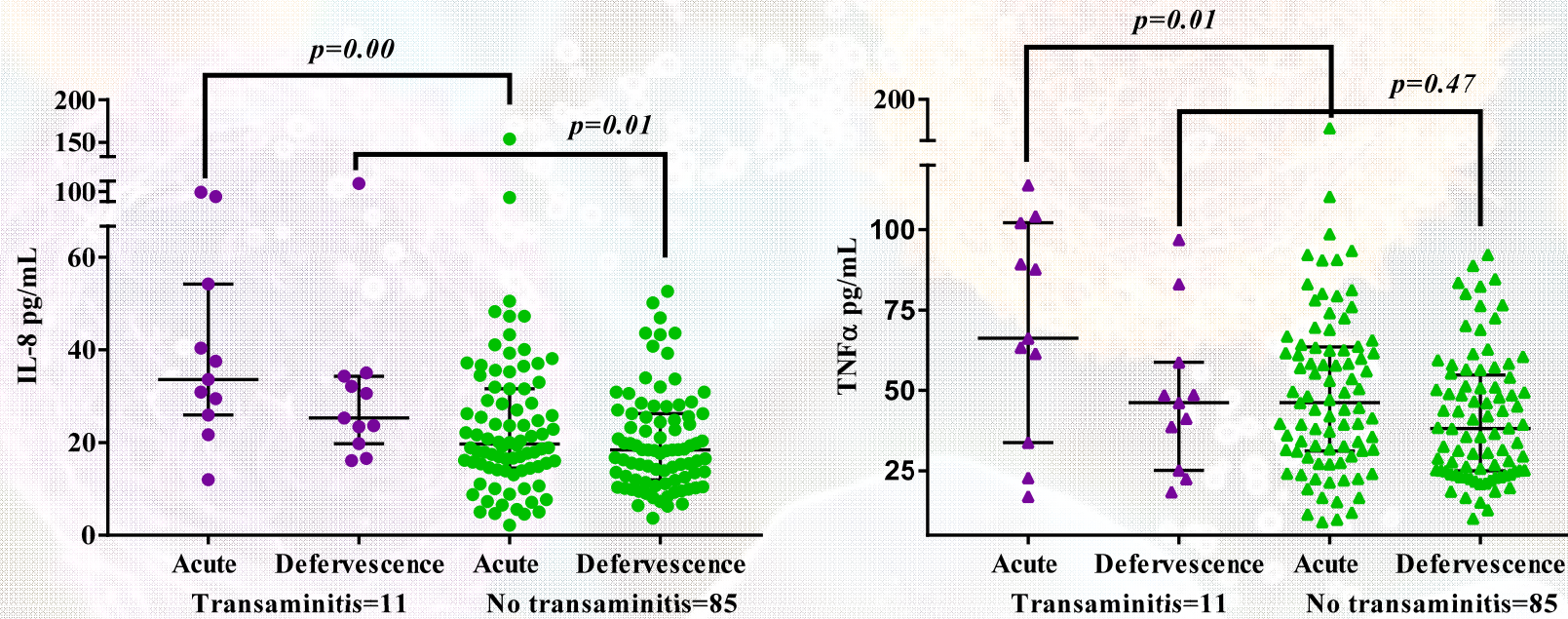
Cytokine expression during the three phases of dengue infection



IL-6 and IL-8 expressions with bleeding during the acute phase and at defervescence



IL-8 and TNF α expressions with transaminitis during the acute phase and at defervescence



Conclusion

- Secondary infections causes a robust T-helper 2 response
- Cytokine expression \uparrow DHF vs DF
- IL-8 elevation suggest its role with bleeding in dengue infection

Limitation

- Most of the subjects were of mild to moderately severe
- Other criteria's for DHF not accounted for

Acknowledgement

Assistant Professor Weerapong Phumratanaprapin
Associate Professor Benjaluck Phonrat
Professor Srisin Khusmith
Professor Terapong Tantawichien
Associate Professor Kesinee Chotivanich
Dr. Prakaykaew Charunwatthana
Dr. Sant Muangnoicharoen

BIKEN

Professor Eiji Konishi
Assistant Professor Atsushi Yamanaka
Mrs. Duangjai Changtong
Ms. Varaporn Pongcharoen

Mahidol Osaka Center for Infectious Disease (MOCID)

Professor Tatsuo Shioda
Dr. Emi Nakayama and her staff

Tropical Medicine Diagnostic Reference (TMDR) laboratory

Assistant Professor Pornsawan Leungwutiwong and her staff

Center of Excellence for Antibody Research (CEAR)

Associate Professor Pongrama Ramasoota and his staff

Staff at the Hospital for Tropical Diseases and at the Department of Clinical Tropical Medicine

Assistant Professor Watcharapong Piyaphanee
Assistant Professor Udomsak Silachamroon
Associate Professor Yupaporn Wattanagoon
Professor Sasithon Pukrittayakamee
Associate Professor Emsri Pongponratn

Professor Yaowalak Sukthana for the two scholarships awarded by her for this PhD research, 2015 Dean MORU and Dean MOCID/BIKEN scholarships