

University of Maryland Baltimore Graduate School

## Announcement of Doctoral Dissertation Defense\*

Candidate: Suntara Eakanunkul

Date, Time, and Place: November 15<sup>th</sup>, 2007, 10.00 A.M., HSF II Room 600

Dissertation Title: Characterization of the Periplasmic Heme-Binding Protein, ShuT, from *Shigella dysenteriae*

Dissertation Abstract\*\*:

Iron is required in bacteria as an essential element for their survival and virulence. To establish infection in the host, bacteria have to acquire iron in the form of heme or heme-containing proteins. Several bacterial pathogens have developed heme acquisition systems in order to utilize heme directly from the host. The heme utilization system includes a membrane receptor, a periplasmic binding protein, and an ABC transporter complex. In *Shigella dysenteriae*, the *Shigella* heme uptake (*shu*) locus has been identified. In the current study we have characterized the periplasmic heme-binding protein, ShuT from *S. dysenteriae* at biochemical and structural levels. ShuT is a monomeric protein with a molecular weight of 28.5 kDa and can bind heme with very high affinity. The UV-vis, resonance Raman, and MCD spectroscopic techniques together with the sited-directed mutagenesis indicate that ShuT is a five-coordinate high spin ferric heme with Tyr-94 as the proximal ligand. In addition, the crystal structure of ShuT has been solved. The overall fold of ShuT structure is similar to that of BtuF, a vitamin B12 transport protein of *E. coli*, which has two globular domains connected with a long rigid  $\alpha$ -helix, typical characteristic of class III periplasmic binding protein. The heme binding pocket of the ShuT crystal reveals the proximal heme ligand to be Tyr-67 (Tyr-94 in amino acid sequence) as expected. The current study also involved the screening of small molecule inhibitors of the bacterial heme oxygenases (*nm*-HO and *pa*-HO). Lead compounds have been identified which will provide a basis for the future development of potential novel antimicrobials specifically targeting the heme utilization pathway.

Dissertation Committee Chair (name and title): Dr. Angela Wilks, Associate Professor

Dissertation Committee Members (names and titles): Dr. Paul Shapiro, Associate Professor  
Dr. Sarah Michel, Assistant Professor  
Dr. Yuan Luo, Associate Professor  
Dr. Iqbal Hamza, Assistant Professor

\*The Open Presentation is open to the university community and invitees of the candidate. Any member of the Graduate Faculty may observe the Final Examination. Only committee members may vote. For more information, see **Procedures for Examination of the Doctoral Dissertation.**

\*\*You must type your abstract on this form in the space provided.

Updated: February 24, 2006