NANYANG TECHNOLOGICAL UNIVERSITY

School of Biological Sciences

Reg. No. 200604393R

Research Theme:

Research Project Title: **The role of RNA modifications in malaria parasite biology**

Principal Investigator/Supervisor: **Prof. Peter Preiser**

Co-supervisor/ Collaborator(s) (if any):

Project Description

The post-transcriptional regulation of translation by the dozens of modified nucleosides in RNA – the epitranscriptome – has recently been recognized as a key additional step that impacts on cell function and biology. The epitranscriptome can play a role both at the level of mRNA modifications as well as tRNA modifications. Recent work has shown that the dynamic regulation of tRNA modifications coupled with codon-biased gene families has a direct impact on the translational capacity of a cell. Changes in tRNA modifications have been shown in particular to be important factors in cellular stress responses.

The malaria parasite *Plasmodium falciparum* still remains one of the most important infectious disease globally, causing huge tolls both in terms of morbidity and mortality. The genome of the parasite has revealed a number of striking features including the lack of an extensive transcriptional regulatory capacity as well as a relatively small number of tRNA genes. While all nuclear-encoded tRNAs in *P. falciparum* are similar to other eukaryotic tRNAs in terms of semi-conserved sequences and structure, the parasite has the smallest set of tRNA genes for a eukaryotic cell, with only one gene copy per tRNA isoacceptor for the nuclear genome. This unique characteristic of *P. falciparum* highlights the potential importance of epitranscriptomic modifications in a complex regulatory network that accurately decodes 61 codons by 45 cytoplasmic tRNA iso-acceptors.

To study the role of epitranscriptomics in *P. falciparum* in more detail, we have characterized the dynamic changes of tRNA modifications during the parasite developmental cycle. This data indicates a critical role for tRNA modifications in regulating translation during development. The data also indicates that epitranscriptomics plays an important role in regulating parasite stress responses.

Based on these preliminary data the aim of this project is fourfold:

i. To test the link between codon-biased translation and tRNA modification changes across the IDC.
ii. To validate directly the relationship between tRNA modifications and codon-biased gene translation rates.
iii. To establish the importance of tRNA modifications in parasite stress response.
iv. To identify and validate the main RNA modifying enzymes.

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To address these questions, we will combine a range of systems-level experimental approaches including LC-MS based quantification and characterization of RNA modifications as well as quantitative proteomics. The information obtained will then combined with genetic strategies to identify the enzymes important in regulating these processes. Overall, it is expected that this project will provide new insights on the importance of epitranscriptomic strategies in parasite biology and stress response.

Supervisor contact:

If you have questions regarding this project, please email the Principal Investigator: PRPreiser@ntu.edu.sg

SBS contact and how to apply:

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Please apply at the following:

http://admissions.ntu.edu.sg/graduate/R-Programs/R-WhenYouApply/Pages/R-ApplyOnline.aspx