

Multidimensional quantification of RNA modification dynamics: An integrative approach to study translational reprogramming in pathogenic mycobacteria

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The ultimate goal of this study is to understand how pathogenic mycobacteria utilize RNA modifications to control translation and survive the human innate immunity. Tuberculosis especially, a mycobacterial disease, is thought to latently infect a third of the world's population in its dormant form. Yet, despite the availability of genomic and proteomic knowledge on how the invading pathogen responds to hostile host environments, our ability to understand the gene regulation system in these pathogens is hampered by the lack of understanding of gene expression controls during translation. We present preliminary evidence that the 27 tRNA modifications in mycobacteria undergo stress-induced reprogramming and play a major role in regulating gene expression by controlling selective translation key stress response genes as the organism enters and exits hypoxia-induced dormancy. We initiated these studies with a multidimensional HPLC platform to isolate, purify and quantify all major non-protein coding RNA species and systemically elucidated the complete set of RNA ribonucleoside modifications in *Mycobacterium bovis* BCG with LCMS/MS. When BCG cells were subjected to hypoxia, multivariate statistical analysis led to the discovery of signature changes in the spectrum of tRNA modifications that define each stage of entry into hypoxia-induced non-replicative state and subsequent resuscitation upon exposure to oxygen. Correlative analysis of specific ribonucleosides altered during hypoxia with the proteins expressed at the same time will provide insights into the mechanisms controlling selective gene expression during the cellular response to the host environment, with implications for developing new pathogenesis-relevant functional biochemical assays, therapeutic biomarkers and drug targets.

Biography

Yok Hian Chionh is pursuing his Ph.D. at the School of Medicine in the National University of Singapore as a Singapore-Massachusetts Institute of Technology Alliance for Research and Technology (SMART) graduate fellow. He has degrees in Biological Sciences and Economics. Currently, he is looking at the interplay between tRNA modifications and codon-bias in transcripts and figuring out how selective translation works to regulate gene expression.

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