NUS National University of Singapore | Department of Biological Sciences
Faculty of Science

BIOLOGY COLLOQUIUM

Friday, 15 April 2016 | 4pm | DBS Conference Room 1

Hosted by A/P Liou Yih Cherng



"Ye GADDs, understanding the impact of stress in disease is stressful!"

(Deciphering Role of eIF2α Phosphatases in mRNA Translation)

By **Shirish Shenolikar**
Professor, Duke-NUS Medical School Singapore
& Duke University School of Medicine, USA

The transient repression of mRNA translation is an immediate and universal response of all eukaryotic cells to variety of perturbations in their environment. This "integrated stress response" allows cells to slow general protein synthesis and focus their limited energy resources on translating mRNAs that encode stress proteins. This redirection of protein synthesis is critical for alleviating or overcoming stress and ensuring cell survival. Failure to execute this complex translational and transcriptional response correctly triggers apoptosis and eliminates damaged or dysfunctional cells thereby preserving overall\ tissue function. In large part, stress-mediated repression of mRNA translation occurs through phosphorylation of the eukaryotic translation initiation factor, eIF2α, βψ one or more stress-decoding εΙΦ2α κιναασεσ. Subsequent transcription of the GADD34 gene, which encodes a phosphatase regulatory subunit, assembles an eIF2α phosphatase that restores general protein synthesis and normal cell function. By contrast, the role of another eIF2α phosphatase, containing CReP or Constitutive Repressor of eIF2α Phosphorylation in stress response is still poorly understood. This presentation will review current understanding of protein serine/threonine phosphatases, stress signaling and our recent efforts to utilize transcriptome-wide ribosome foot-printing to decipher to the roles of eIF2α phosphatases in mRNA translation. The work highlights the dramatic impact of stress on the spatial and temporal dynamics of protein synthesis in mammalian cells.

Artwork by Ann Nee, DBS, NUS