

Research Theme:
Research Project Title: Synapse-to-nucleus signaling and transcription-dependent plasticity in neurodegenerative disorders
Principal Investigator/Supervisor: CHNG Toh Hean
Co-supervisor/ Collaborator(s) (if any): NA
Project Description
<p>Transcription and translation of new gene products is critical for establishing and maintaining long lasting memory. To initiate activity-dependent transcription, neuronal inputs that arrive at the synapse must be relayed to the nucleus to trigger changes in gene expression. Many of these synaptic contacts are found in distal neuronal projections far from the soma and as such, neurons have evolved various synapse to nucleus signaling mechanisms for long range transmission of signals. Any failure or deficits in the relay of signals can result in altered activity-dependent transcription which perturbs neuronal function. Not surprisingly, many neurological and neurodegenerative disorders that lead to a loss of cognitive abilities have altered activity-dependent gene expression.</p> <p>In Singapore, dementia is on the rise owing to a sharp increase in the aging population. Neurodegenerative disorder such as Alzheimer's disease (AD) is a leading contributor to dementia for which there is currently no cure. In numerous Alzheimer's disease (AD) mouse models, synaptic dysfunction can be detected prior to the emergence of amyloid plaques of neurofibrillary tangles. These AD mice often exhibit early onset deficits in various learning and memory tasks. Using established AD mouse models, we want to understand the association between synaptic dysfunction, how that impacts synapse to nucleus signaling and changes in transcription-dependent plasticity during early stages of the disease. To that end, we will employ a multidisciplinary approach including, but not limited to cellular and molecular assays, live cell imaging, quantitative proteomics and nuclear profiling of vulnerable population of neurons, etc. The ultimate goal of the project is to elucidate the basic disease mechanisms that underlie the temporal progression of neurodegenerative disorders.</p>
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