Neurobiology/Ageing Programme

SEMINAR

NUS National University of Singapore

Life Sciences Institute

"Oxidative stress, post-translational modifications and neurodegenerative diseases."

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Introduction

Dr. Jin Xu received his Ph.D. degree in Molecular Cellular Biology from Tulane University in 1998, and finished his postdoctoral study on the molecular mechanisms of Alzheimer's and Parkinson's diseases at Harvard Medical School in 2003. Subsequently, he joined the Department of Neurology, St. Elizabeth's Medical Center, Tufts University School of Medicine, as an Assistant Professor to investigate the molecular pathogenesis of Parkinson's disease. In August 2010, Dr. Xu was recruited to the Institute of Neuroscience, Chinese Academy of Science in Shanghai to lead the Lab of Mechanisms of Neurodegenerative Diseases. His current research interests include the mechanisms and translational research of PD and ALS. Dr. Xu was a recipient of the Charlton Research Award, Tufts University School of Medicine (2007) and the "Hundred Men Talent" award from the Chinese Academy of Science in 2011.

Abstract

The accumulation of oxidative insults during aging is a key factor contributing to the development of neurodegenerative diseases, such as Alzheimer's (AD) and Parkinson's diseases (PD). The ability to efficiently remove free radicals is crucial to the survival of neurons. One of the PD-associated protein, DJ-1, is an oxidative stress responsive protein subject to oxidation modification in the AD and PD brains. We have found that DJ-1 is a transcriptional co-activator activating the expression of both the human tyrosine hydroxylase (TH) and MnSOD, thus affecting both the dopaminergic and Redox pathways. Furthermore, the transcriptional regulation of TH and MnSOD requires the suppression of protein SUMOylation by DJ-1. Like ubiquitination, SUMOylation is an ATP-dependent dynamic process requiring the participation of E1 activating enzyme, E2 conjugating enzyme and E3 ligase and affects the cellular distribution, protein interaction pattern and stability of the target proteins. When DJ-1 is oxidized, its ability to suppress SUMOylation is attenuated, leading to decreased expression of mitochondrial proteins involved in the detoxification of free radicals. Our studies present a model where the normal function of a PD-associated protein could be negatively affected by the accumulation of oxidative insults, thus contributing to the development of sporadic PD. In addition to these studies, I will also discuss our ongoing work on the molecular mechanisms of ALS/FTLD.

Date and time: Friday, 13 July 2012
Time: 3.00 – 4.00pm
Venue: NUS Centre for Life Sciences Seminar Room 2
Host: Prof Barry Halliwell, Programme Leader, Neurobiology/Ageing Programme