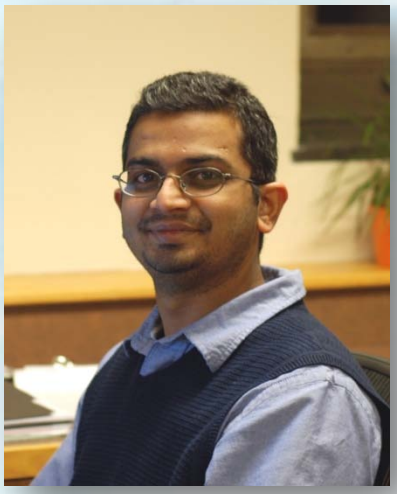
Life Sciences Institute
Neurobiology/Ageing Programme

"Transcriptional regulation of axon growth in the mammalian central nervous system"



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4 October 2013(Friday)

12.00pm

NUS Centre for Life Sciences (Seminar Room 2)

Host: A/P Soong Tuck Wah (Head, Dept of Physiology)

Abstract

Proper axon growth and extension is critical for formation of functional neuronal circuits both during development and for re-establishing connections following injury. Axon growth is mediated by several extracellular signals, which activate a complex network of intracellular effectors including signalling cascades and cytoskeletal proteins at the growth cone, which convey information to critical transcription factors in the nucleus. This growth cone-to-nucleus signalling to coordinate gene expression is critical for sustained axon extension and connectivity both during development and for axon regeneration after injury. A fundamental question remains: what is the nature of the growth cone-to-nucleus signalling and the transcriptional program initiated in the cell soma during axon growth? Towards identifying the genetic control of axon growth in the mammalian central nervous system, we found that the stimulus-dependent transcription factor, serum response factor (SRF) plays a critical cell-intrinsic role in axon growth. Mechanistically, SRF is activated by direct phosphorylation by GSK3 kinase. Axonal growth deficits caused by GSK3 inhibition could be rescued by expression of a constitutively active SRF. The SRF target gene and actin-binding protein, vinculin, is sufficient to overcome the axonal growth deficits of SRF-deficient and GSK3-inhibited neurons. Our findings reveal a novel GSK3–SRF-Vinculin pathway that regulates axonal growth in the central nervous system.

I obtained my Bachelor's degree in Biochemistry from Bharathiyar University and Master's degree in Biotechnology from Madurai Kamaraj University, India. I joined the laboratory of Prof. Wang Yue at the IMCB, Singapore in 1996. My Ph.D. thesis work led to the discovery of iron transporters as a critical virulence factor in the human pathogenic fungus, Candida albicans. In 2001, I joined the lab of Prof. David Ginty in the Department of Neuroscience, The Johns Hopkins University Medical School, Baltimore. My postdoctoral research work identified serum response factor (SRF) as a critical mediator of activity-dependent gene expression, synaptic plasticity and, learning and memory in mice. In 2006, I joined as an Assistant Professor of Neurobiology in the Department of Anatomy and Neurobiology, Washington University School of Medicine, St. Louis, MO. In July 2013, I joined the Centre for Neuroscience, Indian Institute of Science, Bangalore as an Associate Professor. My lab is currently interested in several longstanding questions in developmental neurobiology – understanding the molecular mechanisms regulating axonal growth during development and how these mechanisms can be activated to promote axonal regeneration after injury and towards elucidating the mechanisms regulating neural stem cells to astroglial differentiation in the brain and how these mechanisms might go awry in gliomas.