Date: March 26, 2015 (Thursday)
Time: 12.00 pm – 1.00pm
Venue: MD9, level 1, Workshop 1 & 2

PLS

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PHYSIOLOGY LECTURE SERIES

Mechanisms of polarized sorting in neurons

Abstract

Neurons are highly polarized cells with specialized somatodendritic and axonal domains. Sorting of newly-synthesized transmembrane proteins to each of these domains is in part dependent on selective incorporation of the proteins into distinct populations of vesicular transport carriers in the neuronal soma. We found that sorting to the somatodendritic domain is dependent on recognition of tyrosine-based or dileucine-based sorting signals in the cytosolic tails of the proteins by the clathrin-associated adaptor protein 1 (AP-1) complex. Mutation of the signals or inactivation of AP-1 or clathrin in rat hippocampal neurons abrogate somatodendritic sorting and result in non-polarized distribution of various receptors and transporters. AP-1 inactivation also causes a decrease in the number of excitatory but not inhibitory synapses. This is in part due to a defect in the biogenesis of dendritic spines. We also addressed the question of how the vesicular transport carriers themselves become sorted to the somatodendritic and axonal domains. We found that somatodendritic carriers fail to enter the axon at a region in the axon hillock that we named "pre-axonal exclusion zone" (PAEZ). Tagging of a somatodendritic protein with a peptide motif that binds to kinesin-1 is sufficient to drive transport of whole somatodendritic vesicles through the PAEZ towards the distal axon. On this basis, we propose that polarized sorting of transport vesicles occurs at the PAEZ and depends on the ability of vesicles to acquire an appropriately directed microtubule motor. These studies highlight the roles of the AP-1 complex in the sorting of transmembrane cargos into somatodendritic carriers and of differential recruitment of microtubule motors at the PAEZ in the selective delivery of vesicular transport carriers to the axon or dendrites.

Convener: A/Prof Soong Tuck Wah

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PHYSIOLOGY National University of Singapore