Synapse formation, synaptic plasticity and neurodegeneration: The role of MEN1 gene

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Research Abstract

Defining the fundamental mechanisms that underlie precise neuronal assembly during development, regeneration and synaptic plasticity are critical not only for understanding all nervous system functions, but also for various developmental (e.g. Autism spectrum) and neurodegenerative disorders (e.g. Alzheimer's, Parkinson's etc.) that are met in clinical practice. We have made a seminal discovery that a previously identified tumour suppressor gene (MEN1) controls cholinergic synapse formation and synaptic plasticity. In Lymnaea, we demonstrated that MEN1, activated by neurotrophic factors, regulates the expression of excitatory, nicotinic acetylcholine receptors. Using this highly tractable model, we have characterized and defined

the cellular and molecular pathways underlying synapse formation both in vitro and in vivo following single cell transplantation techniques. Using a rat and a mouse knockout model, we have since demonstrated that MEN1 may similarly regulate synapse formation and synaptic plasticity between cortical and hippocampal neurons, whereas its expression appears to be compromised in a mouse knockout model of Alzheimer's. Using both invertebrate and vertebrate models, we will provide direct insights into the function of MEN1 gene in the regulation and maintenance of synapse in both developing and adult brain cells. Conditional MEN1 knockouts using a mouse line with a Floxed-MEN1 gene by crossing with Cam2K-cre mice will specifically allow us to knockout MEN1 function and using a battery of behavioural tests, we will determine learning and memory deficits in freely behaving animals. We will also examine human tissue obtained from Alzheimer's brain to deduce the expression profiles of MEN1 in concomitant with the expression of trophic factors, their receptors and the nAChRs to provide fundamental insights into the function of a tumour suppressor on one hand, and the neurodegenerative diseases on the other hand.

Further information available at:

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