FEZ1 MODULATES EXCITATORY-INHIBITORY BALANCE BY REGULATING GABAERGIC SYNAPSE FORMATION

Authors and affiliations:

Shi Jun Ng[1,2,3], Huang Hua[1,4], Rachel Koh Woon Sim[5], Soong Tuck Wah[1, 2, 3], Ong Wei Yi[2,5], John Jia En Chua[1,2, 3, 6]

[1]Department of Physiology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore;

[2]LSI Neurobiology Programme, National University of Singapore, Singapore, Singapore.

[3]Healthy Longevity Translational Research Program, Yong Loo Lin School of Medicine, National University of Singapore

[4] Electrophysiology Core Facility, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

[5]Department of Anatomy, National University of Singapore, Singapore, Singapore.

[6]Institute of Molecular and Cell Biology, Agency for Science, Technology and Research (A*STAR), Singapore

Abstract

Proper functioning of the neural circuit depends on the establishment and maintenance of an excitatory-inhibitory imbalance. This process is in turn highly dependent on the formation of precise synaptic contacts by both excitatory and inhibitory neurons. To support synaptogenesis, delivery of synaptic cargoes to nascent synapses to mediate pre- and post-synaptic specialization must be coordinated. Fasciculation and Elongation Protein Zeta 1 (FEZ1), a Kinesin-1 molecular adaptor protein, had been demonstrated to facilitate early axodendritic development and was found to be involved in the transport of synaptic proteins. Collectively, this suggests the possibility that FEZ1 could be essential in regulating synaptogenesis and neural circuit establishment. Supporting this, we show that the loss of FEZ1 strongly delays later stages of dendritic development, corresponding to the formation of synapses in the developing neural circuitry. Interestingly, defects in the formation of GABAergic, but not glutamatergic, synapses were found in FEZ1-deficient neurons. This was accompanied by changes in GABAergic transmission in these neurons. This study highlights the role of FEZ1 in coordinating dendritic development and synaptogenesis to establish an excitatory-inhibitory balance during neural circuit formation.