manitoba neuroscience network

Cellular Mechanisms of Synaptic Maturation: Connecting Development and Degeneration

SEMINAR & VISITING SPEAKER SERIES

DATE
Monday, April 24th, 2023

12:15 PM

LOCATION
Apotex Centre 050

SPEAKER

Timothy Mosca, PhD

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BIO

Tim Mosca is an Assistant Professor of Neuroscience at Thomas Jefferson University in Philadelphia, PA USA where his lab uses the fruit fly Drosophila to understand the principles of synaptic organization. He uses he/him pronouns and received his B.S. from Yale University and his PhD from Harvard University before completing postdoctoral training at Stanford University. Since the opening of his independent lab in 2017, Dr. Mosca has studied the roles of cell surface proteins in synapse maturation and organization of both peripheral and central synapses, explored the mechanisms that underlie synaptic development in central olfactory circuits, and worked to develop novel tools for cell-type specific analysis of synaptic connections in vivo. Dr. Mosca is, most importantly, an educator, serving as the Course Director of the Cold Spring Harbor Laboratories Drosophila Neurobiology course. He strives to create an inclusive environment, in both the lab and in the classroom, so that all students regardless of their background may have a safe space to learn and excel.

ABSTRACT

Among the processes that govern synaptic development and refinement to build the adult nervous system, synaptic maturation is an essential series of events that promotes the transition from nascent, weak synapse to robust, reliable connection. In the absence of appropriate synaptic maturation, weakened synapses persist into adulthood and their presence can underlie neurodevelopmental, neuropsychiatric, and perhaps even neurodegenerative diseases. Despite the importance of this process to normal neurodevelopment, the molecular mechanisms that underlie, and even the precise events comprising, synaptic maturation remain incompletely understood. By studying both central and peripheral synapses in Drosophila, we have uncovered that a distinct set of events constitutes synaptic maturation at neuro-muscular junctions (NMJ) verses olfactory synapses. NMJ synapse maturation is governed by the recruitment of postsynaptic scaffolding and cytoskeletal proteins following initial presynaptic outgrowth and acquisition of a robust behavioral output. Olfactory synapse development is instead governed by the establishment of a mature complement of opposed active zones made by a class of neurons following glomerular neurite growth. We have characterized the events of synaptic maturation in both the CNS and the PNS and began to determine the molecular cascades that influence synaptic maturation. At the NMJ, we have found that multiple cell surface proteins, including the Alzheimer's Disease-linked protelytic complex, gamma-secretase, influence synaptic maturation. Gamma-secretase functions in the non-canonical Wnt pathway to regulate expression of genes associated with synaptic maturation. In the CNS, distinct Alzheimer's-disease linked and cancer-linked cell surface proteins also influence maturation of glomerular circuits and synaptic growth. In characterizing the events of, and molecules promoting, synaptic maturation, the molecular connections between disease-linked genes and basic developmental processes are becoming evident, suggesting that failures in neurodevelopment may precede and influence neurodegenerative events.

For more information:

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