香港中文大學
CUHK

GCNI
Gerald Choa Neuroscience Institute
蔡永業腦神經科學研究所

Research Seminar

Local protein synthesis in axons sustains synapse-specific neurotransmission

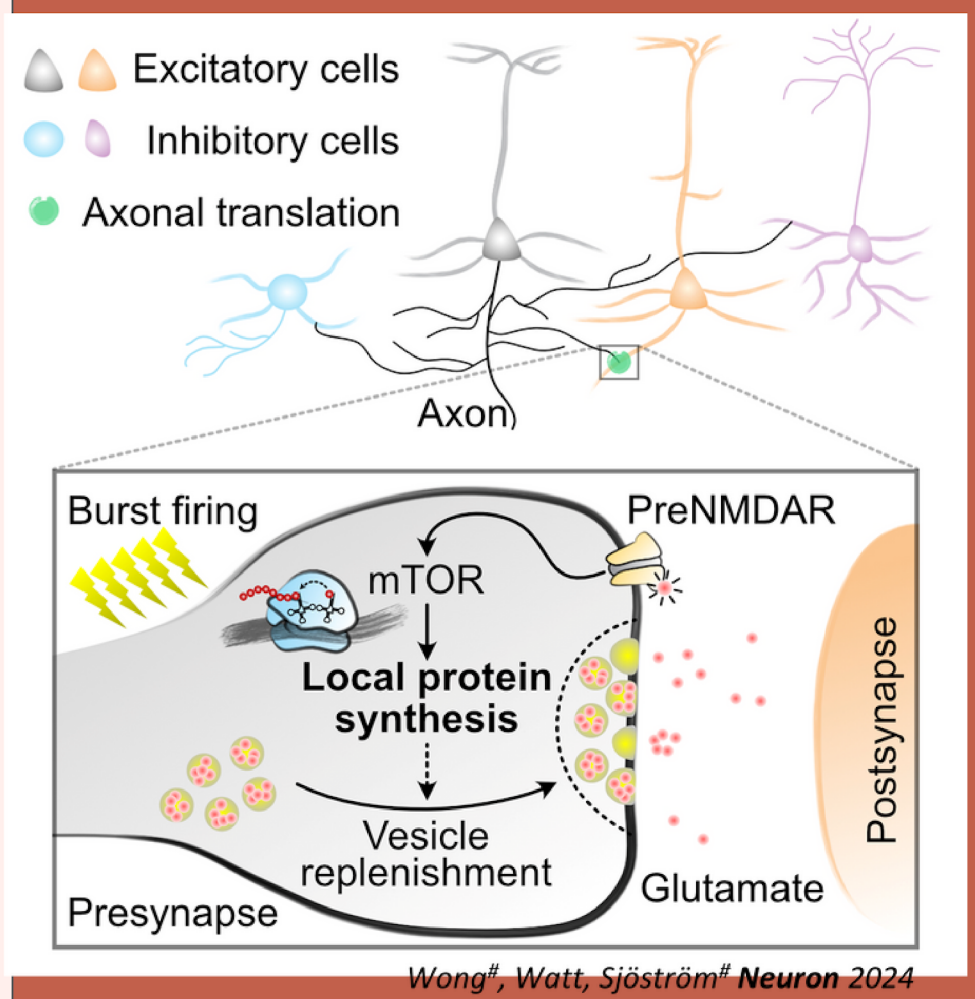
Dr. Hovy Wong completed his undergraduate and MPhil research with Prof. Nancy IP at HKUST, where he examined neuronal kinase signaling. He then studied neurodevelopment and earned his PhD degree under the supervision of Prof. Christine Holt at Cambridge. For postdoctoral training in Prof. Jesper Sjöström's lab at McGill, Hovy uses advanced electrophysiology and custom optics to study neurotransmission and synaptic plasticity.

DR. HOVY WONG

27 Mar 2024 (Wed) 4-5pm

G02, Lo Kwee-Seong IBSB (Area 39)

For more than 60 years, memory formation has been linked to protein synthesis, with the prevalent view that the nascent proteins originate from the cell body. Yet recent omics studies have found hundreds of mRNAs in axons, raising the possibility that presynaptic mRNA translation controls neural communication.



*Wong#, Watt, Sjöström# **Neuron** 2024*

Using quadruple whole-cell recordings, we found that burst neurotransmission at synapses between neocortical layer-5 pyramidal cells depends on protein synthesis linked to presynaptic NMDA receptors and mTOR. We localized protein synthesis to axons with 2-photon laser microsurgery and nascent protein live imaging. We found that translation sustains neurotransmission via controlling the vesicle readily releasable pool size and replenishment rate. We live imaged axons and found sparsely docked RNA granules, suggesting synapse-specific regulation. In agreement, translation boosted neurotransmission onto excitatory but not inhibitory basket or Martinotti cells. Local axonal mRNA translation is thus a hitherto unappreciated principle for sustaining burst neural coding at specific synapse types.

Protein synthesis has emerged as a promising candidate target for treating neuropathologies such as autism spectrum disorder and Alzheimer's disease, yet the focus has historically been postsynaptic. Our results highlight the potential for neuropathology interventions that rely on synapse-type-specific local translation in axons.