IBS Seminar

Super-resolution imaging and tracking of synaptic receptors in live neurons

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In our brain, there are over 100 billion neuron cells that connect as they send and receive signals (electric impulses). These neuronal connections are called synapses, where glutamate receptors, including AMPARs and NMDARs, function to receive signals when glutamate ions have been diffused across the synaptic cleft and bound to them. These receptors serve a significant role in memory, so that it is important to understand their dynamics and the underlying mechanism that creates or deletes memories. I use optical microscopy that allows precise observation of these dynamics; more specifically, I have accurately imaged the dynamics of these receptors using super-resolution fluorescent microscopy and single molecular tracking. Although it is widely accepted that these receptors function in the synapses, it has been a point of some controversy as to where these receptors are located when they are inactive prior to being recruited to receive more signals in the synapse. Previous studies on AMPARs have reported that most were freely diffusive in extra-synaptic regions; however, the previous observations suffered from technical limitations because the researchers labeled AMPARs using big quantum dots. These commercially available qdots are 25 ~ 30 nm in diameter, which is bigger than the gap of the synaptic cleft (20 ~ 25 nm). This explains why the previous results showed the majority of AMPARs to be freely diffusive in the extra-synaptic region. To overcome this problem, we developed smaller qdots that are only 10 nm in diameter. Using these small qdots, the majority of AMPARs were found to be localized in nano-domains of the synaptic region and to be quite stable there for a fifteen-minute period. Previous studies on NMDARs have reported that the placement and dynamics in neurons of the two main subunits (GluN2A and GluN2B) were significantly different, while my research using small qdots showed little difference between the two subunits. The techniques and results that I have developed and obtained will contribute to our understanding of long-term potentiation and long-term depression in the brain.

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