The 152nd iCeMS SEMINAR

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16:30-17:30

Visualizing biochemical reaction at the moment of synaptic memory formation

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Venue: 2nd Floor Seminar Room (#A207)
iCeMS Main Building (#70), Kyoto University

In the central nervous system, most excitatory synapses terminate on dendritic spines, tiny (~0.1 femtoliter) protrusions emanating from the dendritic surface. Ca^{2+} influx into spines activates signaling networks composed of tens of species of molecules to induce diverse forms of synaptic plasticity, which is thought to underlie learning and memory. To further our understanding of signaling mechanisms underlying synaptic plasticity, we have developed a technique to monitor signaling activity in single dendritic spines in slices using 2-photon fluorescence lifetime imaging (2pFLIM) in combination with new FRET sensors extensively optimized for 2pFLIM. Using this technique, we succeeded in monitoring activity of many signaling proteins, including small GTPase proteins HRas, Rac1, RhoA, Cdc42 and Rab4/5/8 and kinases PKC, ERK and CaMKII, during spine structural plasticity. we found that these signaling proteins have distinct spatiotemporal patterns: CaMKII, Cdc42 and Rab4/5/8 activations are restricted to the stimulated spines. In contrary, HRas, Rac1, RhoA and PKC activations spread out of the stimulated spine and diffuse along the parent dendrite over 5-10 µm. Furthermore, following stimulation of 3-7 spines, ERK signaling spreads from the spines into the nucleus and activates transcription factors. Ca^{2+} elevation in the spine, which lasts only for ~0.1 s, is relayed in several different stages. First, Ca^{2+} activates CaMKII, of which activity decays over ~10 s. Then, downstream small GTPase proteins relay this transient CaMKII signal into signals lasting 10-30 min. ERK activity in the nucleus increases over ~20-30 min and sustained for at least 90 min. This rich spatiotemporal regulation must play an essential role in coordinating cellular events occurring within spines and the dendritic shaft and the nucleus to regulate function and structure of dendritic spines.

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