Seminar のご案内

Spatiotemporal Dynamics of G-actin In Cell Motility and Synapse Development

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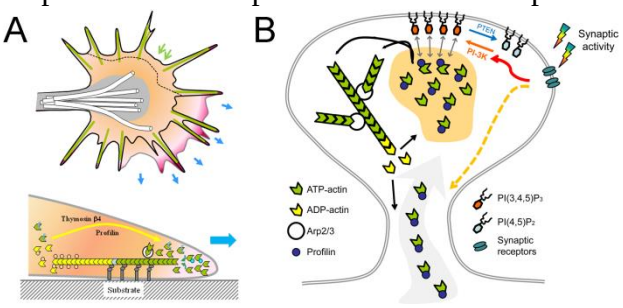
日　時：　2018 年 1 月 22 日（月）　16:00～17:00
場　所：　大セミナー室（Large Seminar Room）

＜**Abstract**＞

The actin cytoskeleton and its dynamic remodeling control and regulate a wide range of neuronal motile activities underlying brain development and function. During early neural development, neurons elaborate axonal projections that depend on the motile growth cones at the tip for their elongation and pathfinding. The growth cone relies on rapid assembly and disassembly of actin filaments (F-actin) for their guided extension to specific targets for precise wiring. Actin monomers (G-actin) are the building block for F-actin but not considered to play a direct role in spatiotemporal control of actin dynamics in growth cones. We recently show that a pool of G-actin dynamically localizes to the growth cone leading edge to drive actin-based membrane protrusion and cell movement. Disruption of this G-actin pool leads to the cessation and retraction of membrane protrusions, and importantly the impairment of growth cone guidance. Our further study demonstrates that spatiotemporal G-actin dynamics also plays a crucial role in synapse development and plasticity. In the vertebrate brain, most excitatory synapses are formed on dendritic spines, the tiny actin-based bulbous protrusions that serve as the postsynaptic platform for synaptic signaling and are modified during learning, aging and neurological disorders. The formation and modification of dendritic spines depend on rapid assembly and dynamic remodeling of the actin cytoskeleton in this highly compartmentalized space. We show that a pool of G-actin is spatiotemporally enriched in dendritic spines, can be regulated by synaptic activity, and plays an important role in spine development and modification. Finally, we provide evidence that the spine enrichment of G-actin depends on the phosphoinositide $PI(_{3,4,5})P_3$. In conclusion, our studies have established a novel actin mechanism by which spatiotemporal regulation of actin monomer concentrations controls actin-based motility underlying brain development and function.



＜**Reference**＞

1. Lee CW, Vitriol EA, Shim S, Wise AL, Velayutham RP, and Zheng JQ (2013). Dynamic localization of G-actin during membrane protrusion in neuronal motility. *Current Biology* 23(12):1046-1056.
2. Vitriol EA, McMillen LM, Kapustina M, Gomez SM, Vavylonis D, and Zheng JQ (2015): Two functionally distinct sources of actin monomers supply the leading edge of lamellipodia. *Cell Reports.* doi: 10.1016/j.celrep.2015.03.033.
3. Lei W, Myers KR, Rui Y, Hladyshau S, Tsygankov D, and Zheng JQ (2017): Phosphoinositide-dependent enrichment of actin monomers in dendritic spines regulates synapse development and plasticity. *Journal of Cell Biology* 216(8):2551-2564.

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