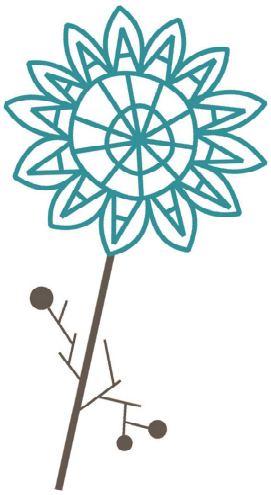
Activity-dependent neuronal circuit formation in the developing cortex



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●Date: September 7 (WED) from 5:30 p.m. 平成 28 年 9 月 7 日（水）17:30～

●Place: Lecture room 2, Medical Education & Library Building 3F
医学教育図書棟3階　第2講義室

ABSTRACT

We are interested in how neuronal circuits remodel during development. Axon branching reflects the remodeling processes. Our previous studies have demonstrated that neuronal activity promotes branch formation of thalamocortical (TC) axons in the developing cortex. We have also shown both activities in target cortical cells (postsynaptic cells) and growing TC axons (pre-synaptic cells) are required for it. However, the molecular mechanisms which underlie activity-dependent TC axon branching remain unknown. To address this issue, we searched for the molecules which are expressed in an activity- dependent manner, and performed loss-of-function and gain-of-function analyses in vivo and in vitro. As for the postsynaptic cell mechanism, we found that the netrin family member, netrin-4 is expressed in cortical cells with activity dependence and promotes axon branching of TC neurons which express the receptor Unc5B. Evidence further indicates that Kit ligand whose expression in the cortex is down- regulated by neuronal activity inhibits branch formation via c-kit receptor which is expressed in TC axons. As for the presynaptic mechanism, we have found that neuronal activity induces nucleocytoplasmic translocation of histone deacetylase 9 (HDAC9), which promotes TC axon branching. These findings suggest that positive and negative regulators are expressed in pre- and post-synaptic cells in response to neuronal activity, and contribute to branch formation of TC axons.

References

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