

**Molecular mechanisms for calcium-mediated refinement of  
competitive synaptic wiring in the brain**

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**【Outline of survey】**

Synaptic circuits in neonates are characterized by excess, overlapping and entangled wiring. These immature circuits are refined into functional and mature ones through use-dependent and activity-dependent strengthening and weakening/elimination of immature synapses. Through this process, almost all of higher brain functions develop robustly during sensitive or critical period of early postnatal life, including cognition, language, music performance, sports, intelligence, thought, personality, and sociality in the case of human beings. Now we understand that the activity dependent synaptic circuit development is facilitated by glutamate receptor activation and subsequent calcium influx into postsynaptic neurons. However little is know about how calcium influx regulates competitive synaptic development. In this research project, we aim to clarify this issue by focusing on calcium-dependent kinases and phosphatases using neuroanatomical, electrophysiological, and developmental biological technologies.

**【Expected results】**

Through this research project, it is expected that the mechanisms by which synapses used during critical period are strengthened and unused ones are weakened and eliminated, will be clarified. This will contribute to our current understanding on critical period development and plasticity of neuronal circuits.

**【References by the principal investigator】**

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- Ichikawa, R., Miyazaki, T., Kano, M., Hashikawa, T., Tatsumi, H., Sakimura, K., Mishina, M., Inoue, Y., Watanabe, M. (2002) Distal extension of climbing fiber territory and multiple innervation caused by aberrant wiring to adjacent spiny branchlets in cerebellar Purkinje cells lacking glutamate receptor GluR  $\delta$  2. **J. Neurosci** 22:8487-8503.

**【Term of project】** FY2007– 2011

**【Budget allocation】** 23,700,000 yen

(2007 direct cost)

**【Homepage address】**

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