Molecular and cellular mechanisms underlying fear memory regulation

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1. Adult Neurogenesis Modulates the Hippocampus-Dependent Period of Associative Fear Memory (Kitamura et al., Cell, 139, 814-827, 2009)

Acquired memory initially depends on the hippocampus (HPC) for the process of cortical permanent memory formation. The mechanisms through which memory becomes progressively independent from the HPC remain unknown. In the HPC, adult neurogenesis has been described in many mammalian species, even at old ages. Using two mouse models in which hippocampal neurogenesis is physically or genetically suppressed, we show that decreased neurogenesis is accompanied by a prolonged HPC-dependent period of associative fear memory. Inversely, enhanced neurogenesis by voluntary exercise sped up the decay rate of HPC-dependency of memory, without loss of memory. Consistently, decreased neurogenesis facilitated the long-lasting maintenance of rat hippocampal long-term potentiation *in vivo*. These independent lines of evidence strongly suggest that the level of hippocampal neurogenesis play a role in determination of the HPC-dependent period of memory in adult rodents. These observations provide a new framework for understanding the mechanisms of the hippocampal-cortical complementary learning systems.

2. Input-specific spine entry of soma-derived Vesl-1S protein conforms to synaptic tagging (Okada et al., Science, 324, 904-909, 2009)

Late-phase synaptic plasticity depends on the synthesis of new proteins which must function only in the activated synapses. The synaptic tag hypothesis requires input-specific functioning of these proteins after undirected transport. To confirm this hypothesis, biochemical tagging activity and an example protein which behaves as the hypothesis predicts should be specified. We found that soma-derived Vesl-1S (Homer-1a) protein, a late-phase plasticity-related synaptic protein, prevailed in every dendrite, and did not enter spines. N-methyl-D-aspartate receptor activation triggered input-specific spine entry of Vesl-1S proteins, which met many criteria for synaptic tagging. These results suggest that Vesl-1S is the first protein supporting the hypothesis and that the activity-dependent regulation of spine entry functions as a synaptic tag.

CARRICULUM VITAE

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EDUCATION

1979	Award the degree of Bachelor of Agriculture, Nagoya University, Nagoya, Japan.
1979-198 4	Graduate School of Agriculture, Nagoya University, Nagoya, Japan.
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RESEARCH EXPERIENCE

1984-1985	Postdoctoral research fellow, Faculty of Agriculture, Nagoya University, Nagoya, Japan.
1985-1991	Researcher, Mitsubishi Kagaku Institute of Life Sciences, Tokyo, Japan.
1991-1993	Research Associate, Howard Hughes Medical Institute, College of Physicians and Surgeons, Columbia University, New York, USA.
1993	Research Associate, New York State Psychiatric Institute, USA
1993-2001	Senior Researcher, Mitsubishi Kagaku Institute of Life Sciences, Tokyo, Japan.
1999-2001	Visiting Associate Professor, Waseda University, Tokyo, Japan.
2001-2009	Group Director, Mitsubishi Kagaku Institute of Life Sciences, MITILS, Tokyo, Japan.
2001-2009	Visiting Professor, Yokohama National University, Yokohama, Japan.
2009-present	Professor, Department of Biochemistry, Faculty of Medicine, Graduate School of Medicine & Pharmaceutical Sciences, University of Toyama, Toyama, Japan

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