論文内容の要旨

Imaging Neural Plasticity Related to Salt Chemotaxis Learning in *Caenorhabditis elegans*

(線虫*C. elegans*の塩走性学習に関わる神経可塑性の可視化)

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Learning and memory is crucial for animals to cope with constantly changing environment. Likewise, the soil nematode *Caenorhabditis elegans* shows various kinds of learning and memory such as thermotaxis learning, odor-starvation associative learning and salt chemotaxis learning. Although molecular mechanisms underlying these behavioral plasticities have been characterized well, how neural circuit shows neural plasticities is mostly unknown. In this study, I focused on salt chemotaxis learning and analyzed neural plasticities using *in vivo* imaging techniques.

C. elegans shows chemotactic behavior toward NaCl. However, it learns to avoid NaCl after prolonged exposure to NaCl for 10-60 minutes under the starvation condition, which is called salt chemotaxis learning. But in the presence of food or serotonin (5-HT), the latter of which is suggested as a food mediator, salt chemotaxis learning does not occur. Therefore, these previous studies suggested that two pieces of information, NaCl and starvation, are integrated in salt chemotaxis learning. As one of molecular mechanisms, insulin-like signaling is important for this behavioral plasticity. The insulin-like signaling is composed of *ins-1*, *daf-2* and *age-1*, which encode an insulin-like peptide, insulin receptor and PI 3-kinase, respectively. The insulin-like peptide INS-1 is secreted from several neurons including AIA, and the downstream signaling proteins DAF-2 and AGE-1 function in one of the major NaCl-sensing sensory neurons, ASE right (ASER). However how neurons including ASER show neural plasticities remained to be elucidated.

First, I introduced an *in vivo* imaging techniques using a microfluidic chip. I measured Ca^{2+} responses and amount of synaptic transmission in ASER. I found that response of ASER increased whereas its synaptic release decreased after prolonged exposure to NaCl without food. These changes in the opposite directions were abolished in mutants of the insulin-like signaling, suggesting that insulin-like signaling regulates these plasticities in ASER. Next, I examined the effect of changes in ASER on downstream neurons. The response of one of the downstream interneurons, AIB, decreased profoundly after NaCl conditioning. I confirmed that synaptic connectivity from ASER to AIB is excitatory by stimulating ASER specifically. This result suggested that strong decrease in AIB was due to decrease in the amount of synaptic transmission from ASER.

These results suggest that the place for integration of two pieces of information, NaCl and insulin-like signaling, latter of which is suggested to transmit starvation signal, is ASER sensory neuron.