Neural Circuit of Multisensory Integration RIKEN Hakubi research team（2021）
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(0) Research field

CPR Subcommittee: Biology

Keywords: Nervous system, temperature, smell, *C. elegans*, behavior

(1) Long-term goal of laboratory and research background

We are all exposed to environmental stimuli in nature. In order to survive and live a high-quality life, all animals need to make the best behavior choice by sensing environmental cues and integrating the information with individual's experience, knowledge and situation. In our lab, we have been investigating the molecular and the neural mechanisms by which animals process sensory information in the brain and make behavior decision. *C. elegans* has a rather simple nervous system and the transparent body, that enables us to observe behavior and neural activities simultaneously. We thus use *C. elegan*s for behavior and calcium-imaging assay that are aimed to identify the entire neural circuit and molecules that regulates sensory integration and behavior decision. For identification of molecules of sensory integration, we'll perform candidate-screening on the mutants of neurotransmitters and non-biased screening with mutagenesis on behavior experiments. With genetic approaches, we will artificially modify the activities of the candidate neurons and/or the expression level of candidate genes to reveal their function in sensory integration. Since most of the genes are evolutionally conserved, we expect that our research can elucidate the universal sensory processing mechanism of nervous system at the level of single neuron and single molecule.

(2) Current research activities (FY2021) and future plans

(A) Investigation of the mechanism of sensory integration of odor and temperature in *C. elegans*

Odor and temperature are important sensory cues for *C. elegans*. *C. elegans* are sensitive to odor to find food and avoid noxious chemicals, and migrate toward an attractive odor, which behavior is known as chemotaxis. Because *C. elegan*s lives in the soil, its' body temperature depends on the location and the environment, and is also sensitive to temperature. *C. elegans* memorizes its cultivation temperature as favorable temperature and migrate toward the direction when it's located on the temperature gradient within the physiological temperature range of 12-26 ºC (thermotaxis). In our experiments, we expose *C. elegans* to attractive odor and temperature stimuli at the same time to investigate the mechanism to integrate these information to produce behavior. Previously, we found that *C. elegans* migrates toward an attractive odor, isoamylalcohol (IAA) when the environmental temperature is around it's cultivation temperature, however, their chemotaxis toward IAA is suppressed at the higher temperature than cultivation temperature by 3ºC or more (Fig).

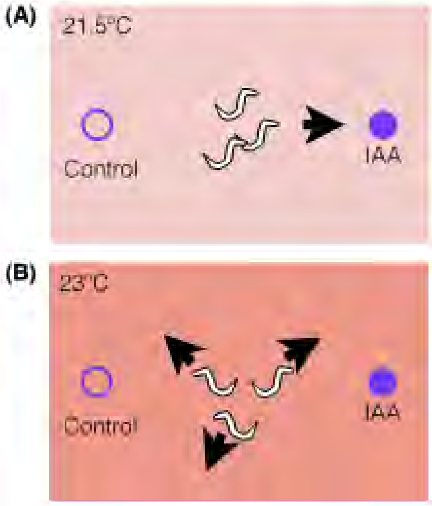

Fig Results of IAA-chemotaxis of *C. elegans* that were cultured at 20°C
A: Worms migrate toward IAA at 21.5°C.
B: Worms migrate randomly at 23°C.

In FY2021, we conducted candidate screening and forward-genetic screening with mutagenesis. We completed screening 9000 mutants and succeeded to isolate 4 mutants that show strong chemotaxis toward IAA even at 25ºC (cultivation temperature = 20ºC). We also completed building up the microscope to monitor a single neural activity with GCaMP on the freely moving *C. elegans* as well as generation of imaging strains that express GCaMP6s in a specific neuron that are known to be involved in thermotaxis and chemotaxis.

Future plan, 1) We will identify the responsible neuron(s) and gene(s) that is required to suppress worm chemotaxis at higher temperature by analyzing mutants that were identified by screening. We also continue forward-genetics screening to complete 30000 strains that cover 95% of *C. elegans* genome. 2) We'll perform calcium imaging assay on freely-moving animals at the same condition as behavior experiments to identify the neurons that alter the chemotaxis toward IAA at a higher temperature. 3)We will analyze the behavior and the calcium imaging data mathematically, and generate simulation model to understand the general mechanism of the behavior choice.

(B) Investigation of the mechanism to acquire high temperature resistance

Each animal has evolved the sensory mechanisms in order to adapt to the environment. Nematode family lives all over the world and is one of the most succeeded animal phylum in terms of the variety of species. Each species has physiological temperature range that matches to its living environment. We are investing how *C.elegans*, one of the nematode, adapts to its physiological temperature, and how it acquires temperature resistance when their environmental temperature changes. Previously, we cultured wild-type *C. elegans* at the highest physiological-temperature (26ºC) that few of them can survive. We continuously cultured those survivors for more than 10 generations at 26ºC, and succeeded to obtain the 'heat-resistant strain' that looks healthy and can produce good number of offspring even at 26ºC.

In FY2021, we analyzed whole genome-sequence of the heat-resistant strains, original strains, and 20ºC kept strains, and obtained the list of mutations found in heat-resistant strains. We purchased mutant strains for some of genes in the list, and monitoring survival of them at 26ºC in order to identify the responsible gene that induce heat-resistance.

Future plan, 1) We will test all the mutants of the candidate genes to identify the essential genes for heat-resistance. 2) We will investigate the epigenetic changes in the heat-resistant strain to identify the candidate genes that contribute to heat resistance. 3) From the genome database of various nematode species, we'll identify the homologue of the genes identified by 1) and 2). We'll then investigate the correlation of the 'heat-resistance' gene expression and the physiological temperature range of various species. We'll also compare the results with Arabidopsis (experiment of acquiring temperature resistance is conducted by Dr. Seki's lab), and reveal the universal mechanisms of adaptation to high temperature.

(3) Members

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(4) Representative research achievements

1. Takeishi, A., 'Environmental-temperature and internal-state dependent thermotaxis plasticity of nematodes', Current Opinion in Neurobiology, 74:102541, 2022

2. Galatsis, K.N., **Takeishi, A**. Insulin Signaling Acts Extensively in *C. elegans* Starvation-Associated Learning and Behavioral Plasticity. J Cell Sci Therapy, S5:315, 2021

Supplementary

Lab members (as of Mar 2021)

Laboratory Homepage

https://cbs.riken.jp/en/faculty/a.takeishi/