Neural Circuit of Multisensory Integration RIKEN Hakubi research team（2020）

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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 together. 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 (FY2020) and plan (until Mar. 2025)

(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 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 °C (thermotaxis). In our experiments, we expose *C. elegans* to attractive odor and temperature stimuli at the same time to investigate the mechanism to integrate those information to produce behavior.

In FY2020, we conducted behavior experiments on *C. elegans* by exposing them to attractive odor, isoamylalcohol (IAA) on thermal plate. We cultured C. elegans at 20ºC and located them onto various temperature gradient with IAA on the opposite side from the cultivation temperature to see how the behavior toward IAA is affected by temperature. We found that at the higher temperature gradient than cultivation temperature (22-26ºC), C. elegans ignores IAA and migrate toward colder side toward cultivation temperature, that indicates temperature information is prioritized to odor (FigA). In addition, we exposed *C. elegan*s to IAA on even-temperature plate, and found that *C. elegans* migrates toward IAA at 21.5ºC but not at 23ºC (Fig B&C). These results suggest that *C. elegans* weights and takes balance of temperature and odor information to produce behavior, and the signaling pathway of IAA sensation might be suppressed at higher temperature than cultivation temperature.

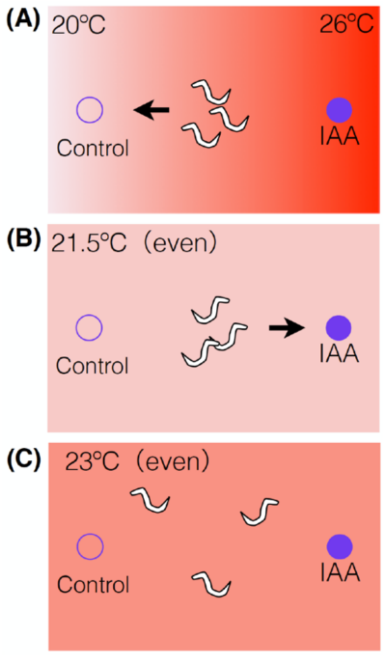


Fig Result of behavior assay on *C. elegans* cultured at 20°C
A: At higher temperature gradient than cultivation temperature, temperature information is prioritized to odor. **B:** At even temperature plate of 21.5°C, *C. elegans* migrate toward IAA. **C:** At even temperature of 23°C, *C. elegans* migrate randomly.

We also (almost) completed to build up the microscope set ups to monitor neural activity with GCaMP on the freely moving *C. elegans*.

Future plan, 1) We will monitor neural activities together with the locomotion of *C. elegans* in the same condition as behavior experiments. For monitoring neural activities, we'll use genetically encoded calcium sensor, GCaMP6. We'll first focus on neurons that are known to be involved in the IAA and/or temperature sensation. 2) We'll perform behavior assay and calcium imaging on the mutants of neurotransmitters to identify molecules required for sensory integration (candidate screening). 3) We'll go on forward genetic screening with mutagenesis to identify molecules that contribute to integrate temperature and odor information.

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

Temperature sensation is essential for survival of all the animals, and each animal has evolved the sensory mechanisms by adapting them to their 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 it's physiological temperature, and how it acquires temperature resistance when their environmental temperature changes.

In FY2020, we cultured wild-type *C. elegans* at various temperature to find the highest temperature (26°C) that few of them can survive. We continued culturing those survivors for more than 10 generations at the highest temperature, and succeeded to obtain the 'heat-resistant strain' that are resistant to the highest temperature that can produce good number of offspring.

Future plan, 1) We investigate the genome editing and/or epigenetic change in the heat-resistant strain by next generation sequencing to identify the candidate genes that contribute to temperature resistance. 2) By genetic approach, we'll identify the genes that contribute to temperature resistance from the candidates of 1). 3) From the genome database of various nematode species, we'll identify the homologue of the gene identified by 2). We'll investigate the correlation of the 'heat-resistant' gene expression and the physiological temperature range of each 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 mechanism of acquiring temperature resistance.

(3) Members

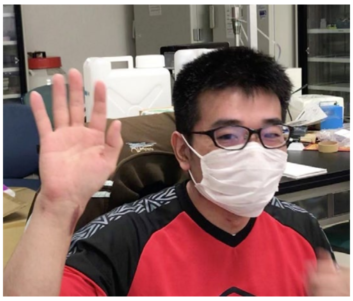
(RIKEN Hakubi Team Leader)
Asuka Takeishi
(Research Scientist (affiliated to CBS))
Yuki Aoki
(Technical Staffs (affiliated to CBS))
Masami Shima, Kristina Galatsis
(Part-time technical Staff)
Kazuko Yahagi

(4) Representative research achievements

1. Yeon, J., **Takeishi, A.**, Sengupta, P. Chronic vs acute manipulations reveal degeneracy in a thermosensoty neuron network. *microPublication Biology*, 10.17912/micropub.biology.000355., 2021
2. **Takeishi, A.**, Yeon, J., Harris, N., Yang, W., Sengupta, P. Feeding state functionally reconfigures a sensory circuit to drive thermosensory behavioral plasticity. *eLife*, 61167. PMCID: PMC7644224, 2020
3. **Takeishi, A.**, Takagaki N, Kuhara A., Temperature signaling underlying thermotaxis and cold tolerance in *Caenorhabditis elegans*, *Journal of Neurogenetics*, pp351-362, 2020.
4. **Takeishi, A.**, Yeon, J., Harris, Sengupta, P. Neuronal mechanisms that drive starvation-dependent thermotaxis plasticity in *C. elegans*, The 43th Annual Meeting of the Molecular Biology Society of Japan (Dec., 2020, Zoom)

Supplementary

Lab members


Laboratory Homepage
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