

Generally Physiological

Fleeing heat and light



This month's installment of *Generally Physiological* focuses on mechanisms that govern negative thermotaxis in flies and worms, and how the same neuropeptide acts at distinct sites to control the timing and location of fly metamorphosis.

Of flies that move into the cold

The fruit fly *Drosophila melanogaster*, like other animals, will move from an overly warm location to one with a more moderate temperature. Whether internal or peripheral warmth sensors are more important in this negative thermotaxis has been controversial, with two sets of neurons—anterior cell (AC) neurons located in the head and hot cell (HC) neurons located in the arista (a process arising from the antenna)—proposed to control fruit fly thermal preference. Although AC neurons sense warmth through the TRPA1 channel, the mechanisms whereby

HC neurons sense temperature has been unclear. Ni et al. (2013) determined that HC neurons express GR28B(D), a member of a large family of seven-transmembrane gustatory receptors previously implicated in chemosensation but not thermosensation. Inhibiting vesicular release from HC neurons blocked the rapid response of flies to a steep thermal gradient (exposure for 1 min to a $>5^{\circ}\text{C}/\text{cm}$ thermal gradient running from $\sim 31^{\circ}$ to $\sim 25.5^{\circ}\text{C}$), as did loss-of-function mutation of the gene

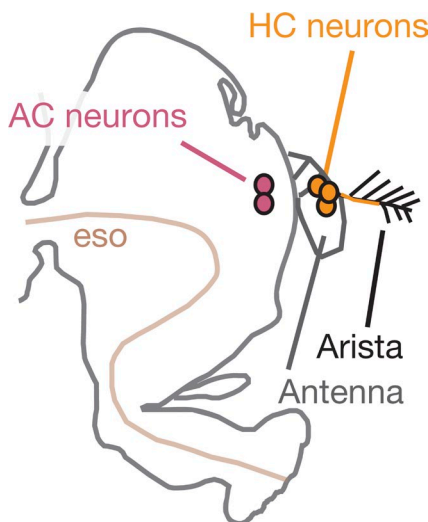
Mechanisms that govern negative thermotaxis in flies and worms, and how a neuropeptide controls the timing and location of fly metamorphosis

encoding GR28B(D), whereas inhibiting release from AC neurons or loss-of-function mutation of *TrpA1* did not. HC-specific expression of GR28B(D) rescued rapid negative thermotaxis with the *Gr28b* mutant, and its ectopic expression in various cell types yielded temperature-sensitive currents and conferred warming-dependent responses and behaviors. Unlike *TrpA* mutant flies, which, as previously reported, were found in regions with unusually warm temperatures ($\geq 28^{\circ}\text{C}$) after a 30-min exposure to shallow thermal gradients, the distribution of flies with the *Gr28b* mutant was indistinguishable from that of wild-type flies under these conditions. The authors thus propose that rapid responses to temperature

fluctuation depend on GR28B(D) in the periphery, whereas internal TRPA1 channels mediate the response to sustained increases in temperature that reach the fly's core.

Defining a thermo-transduction signaling cascade

Like *Drosophila*, *Caenorhabditis elegans* displays negative thermotaxis, and the tiny worms will move from locations warmer than the temperature at which they were cultivated. Warming stimulates thermoreceptor currents in AFD thermosensor neurons; these warming-evoked currents depend on activation of a cyclic nucleotide-gated cation channel and are lost with triple mutation of the genes encoding three receptor guanylate cyclases (GCY-8, GCY-18, and GCY-23) coexpressed in AFD. Remarkably, AFD neurons can detect temperature changes of 0.01°C or less, and AFD thermoreceptor currents exhibit apparent Q_{10} values $>10^{15}$, prompting the suggestion that temperature sensitivity in this system involves a non-linear signal amplification process upstream of channel opening. In this issue, Wang et al. used a combination of genetic and behavioral analyses and in vivo patch-clamp recordings to investigate the signaling network mediating AFD thermotransduction. They determined that GCY-8, but not GCY-18 or GCY-23, was essential for AFD thermoreceptor currents, and identified the phosphodiesterase PDE-2 and the EF-hand protein neuronal calcium sensor 1 (NCS-1, also known as frequenin) as crucial elements of a temperature-sensitive cGMP signaling network that regulates thermoreceptor currents in AFD (Wang et al., 2013).

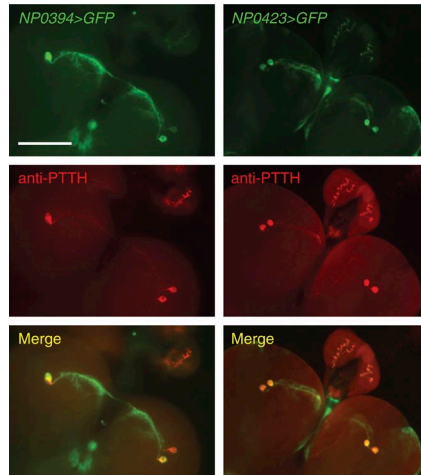


Drosophila head, showing location of AC and HC neurons. eso, esophagus. (Reprinted by permission from Macmillan Publishers, Ltd. *Nature*. Ni et al., 500:580–584, copyright 2013.)

In the right place at the right times

Four neurosecretory cells in the larval *Drosophila* brain project to the prothoracic gland, releasing the neuropeptide prothoracicotropic hormone (PTTH) to stimulate the production and release of ecdysone and thereby the transition to adulthood. This process involves behavioral as well as morphological changes, as the larvae set out to find a site at which to undergo metamorphosis. Yamanaka et al. (2013) determined that these PTTH-producing neurons correspond to the same set of neurons reported to control larval light avoidance. Consistent with a role for PTTH in mediating this response, silencing the *ptth* gene interfered with larval light avoidance. However, whereas knocking down the PTTH receptor Torso in the prothoracic gland blocks ecdysone production, leading to a developmental delay, it failed to affect light avoidance. Noting a marked delay (8–10 h) between inactivation of PTTH-expressing neurons and the effect on light avoidance, the authors determined that PTTH could be detected in hemolymph (consistent with an endocrine function) and

that pan-neuronal *torso* knockdown did, in fact, impair light avoidance. Further analysis revealed *torso* expression in two neuronal populations implicated in light sensing, Bolwig's organ and peripheral class IV dendritic arborization neurons; *torso* knockdown in these neurons interfered



Neurons in the larval *Drosophila* brain implicated in controlling light avoidance (green; expressing *CD8-GFP* under the control of *NPO394-Gal4* or *NPO423-Gal4* drivers) correspond to those immunoreactive for PTTH (red). (From N. Yamanaka, et al. 2013. *Science*. 341:1113–1116. Reprinted with permission from AAAS.)

with light avoidance but failed to affect developmental progression. Calcium imaging indicated that the response to light was diminished by ~25% in *torso* mutant class IV dendritic arborization neurons; further analysis indicated that PTTH and Torso act downstream of photo-sensitive opsins in the light-sensing cells to facilitate TRP channel activation and thereby neuronal depolarization. The authors thus conclude that, in addition to its role in stimulating metamorphosis, PTTH acts at distinct sites involved in light sensing to ensure that it occurs in the dark.

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