Gene discovery explains how fruit flies retreat from heat

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A discovery in fruit flies may be able to tell us more about how animals, including humans, sense potentially dangerous discomforts.

Researchers at Duke University Medical Center uncovered naturally occurring variations of a gene named TRPA1 that is important for the function of pain-sensing neurons throughout the animal kingdom. The gene makes an ion channel, which floods sensory neurons with calcium ions when the fly is near a heat source, causing fruit fly larvae to respond with a corkscrew-style rolling motion away from the heat source (movie link shows an escaping larva).

The team, led by co-authors Lixian Zhong, Ph.D. and Andrew Bellemer Ph.D., of Duke Department of Anesthesiology, found a 37-amino-acid section of nearly four identical protein molecules that controls the

responses of the proteins to temperature. The larvae start their nociception (pain perception) escape roll at just over 100 degrees Fahrenheit (39 degrees Celsius).

Senior author Dan Tracey, Ph.D., associate professor of anesthesiology, cell biology and neurobiology, said these discoveries could have a bearing on injured people with temperature sensitivity in damaged tissues or people with allodynia, who perceive even modest changes in temperature as painful. Even spontaneous pain that occurs in pathological pain states might be explained if the human versions of these channels were to open inappropriately at the normal body temperature, Tracey said.

The work was published in the inaugural issue of *Cell Reports* on Thursday, Dec. 15.

Interestingly, the authors found that the version of TRPA1 that is necessary for detecting the painful temperatures was not a direct temperature sensor. Tracey said this discovery suggests that TRPA1 channels may play an important role in sensing other kinds of pain besides temperature.

The four proteins vary in only two small sections. The scientists were able to find a 37-amino acid section in two of the variants that was important for sensing hot temperature.

Interestingly, many noxious chemicals that trigger painful sensations, including wasabi and tear gas, also activate the TRPA1 channel in humans and fruit flies. The variants identified by the Duke team all respond to these noxious chemicals but vary in their responses to temperature. Finding similar variants in humans may give important insights into pain-sensing.

"Typically heat responses of nociception channels are tested with artificially made mutants, but our study involved four natural gene variants, two of which were related to the avoidance behavior we could observe under the microscope," said Tracey, who directs the Molecular Pain Signaling Laboratory at Duke. "Because evolution created these variants, we had more confidence that the amino-acid section we found was particularly important. We had clues there were unknown versions of this gene, so we were pleased to find the relevant part of the proteins that allows for heat-sensing and nociception."

Provided by Duke University Medical Center