# Worms control lifespan at high temperatures

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The common research worm, *C. elegans*, is able to use heat-sensing nerve cells to not only regulate its response to hotter environments, but also to control the pace of its aging as a result of that heat, according to new research at the University of California, San Francisco.

The new findings have turned upside down a widespread assumption about how cold-blooded animals respond to and regulate heat, the researchers say. The study is reported in the online early edition of the journal "Current Biology" and is available at http://www.cell.com/current-biology/home.

Researchers have known for years that cold-blooded animals, or ectotherms, go through life more quickly at high temperatures than at low temperatures, according to UCSF Professor Cynthia Kenyon, PhD, who was senior researcher on the paper.

At temperatures of 25 degrees Celsius and above, worms move, eat and digest food faster, mature faster and age faster than their counterparts at a more normal 20 degrees. The common assumption, she said, is that the accelerated aging process at higher temperatures occurred passively, in much the same way that a chemical reaction speeds up at higher temperatures.

"We've shown it's not so simple," said Kenyon, a professor in the UCSF Department of Biochemistry and Biophysics and director of the Larry L. Hillblom Center for the Biology of Aging at UCSF. She is renowned for her ongoing research on *C. elegans* (*Caenorhabditis elegans*) and aging.

Humans and other warm-blooded animals have a mechanism that enables us to maintain a constant temperature as our environment heats up or cools. Kenyon said most textbooks explain that worms and other ectotherms cannot do that.

"It's true that worms don't regulate their body temperature, but they do regulate their response to high temperature, slowing down processes that would otherwise go much faster. In fact, they even use steroid hormones to do this, just as we do to regulate our temperature," she said, noting that this might have been a very early evolutionary link between cold- and warm-blooded animals.

*C. elegans* has been known to have thermosensory or heat-sensing neurons, which allow the worms to move towards temperatures they associate with food. If the "chemical reaction" theory were accurate, worms at a constant hotter temperature would age at the same fast rate, whether their thermosensory neurons perceived the heat or not.

The researchers found that when they either killed the heat-sensing neurons or deactivated the worm's genes that produce steroids, the worms had an even greater response to the heat, and as a result aged and died much faster than their counterparts with active neurons. The authors conclude that these heat-sensing neurons actually help the worm regulate its response to increasing heat.

The data suggest that these thermosensory neurons affect lifespan at warm temperature by changing the activity of a steroid signaling pathway, which in turn affects longevity, according to the paper. Specifically, the authors suggest that at high temperature, the worm's thermosensory neurons produce a signal that stimulates expression of the daf-9 gene, which produces a steroid hormone that extends lifespan.

The researchers propose that this thermosensory system allows *C.*

*elegans* to reduce the effect that warm temperature would otherwise have on the processes that affect aging, which is something that warm-blooded animals do by controlling the temperature itself.

This system may allow the animal to maintain a more normal rate of aging even if the temperature rises, Kenyon said.

Previous research also has linked the rate of aging in mammals with temperature. If mice are tricked into thinking that they are in a hot climate, they lower their body temperature and live longer.

While similar steroid hormone pathways exist in humans, Kenyon stressed that, at least for now, this research is more relevant to our general understanding of biology than to any human biomedical connection.

"These findings probably won't result in a new cure for cancer or Alzheimer's," she said. "But they may force us to rewrite the section on cold-blooded animals in high school biology textbooks."

Source: University of California - San Francisco