Biologists find optimistic worms are ready for rapid recovery

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For the tiny soil-dwelling nematode worm Caenorhabditis elegans, life is usually a situation of feast or famine. Researchers at the California Institute of Technology (Caltech) have found that this worm has evolved a surprisingly optimistic genetic strategy to cope with these disparate conditions--one that could eventually point the way to new treatments for a host of human diseases caused by parasitic worms.

As reported in a paper published in the February 26 issue of Science Express, Paul W. Sternberg, the Thomas Hunt Morgan Professor of Biology at Caltech and an investigator with the Howard Hughes Medical Institute, along with postdoctoral scholar L. Ryan Baugh, looked at the worms' genetic response to conditions of scarcity and plenty.

In dozens of batches of the worms, consisting of tens of millions of individuals, Baugh, now an assistant professor at Duke University, synchronized hatching, so that all of the animals in each batch emerged from their eggs at the same time.

Some of the hatched worms were allowed to develop under conditions with scarce nutrients, and others with plentiful nutrients. At precise time intervals (3, 6, 9, 12, and 15 hours after hatching), subsets of both populations were killed en masse and ground up. Their messenger RNA--the genetic material that is produced upon the activation of genes and then translated to produce proteins--was harvested and analyzed at Caltech's Jacobs Genetics and Genomics Laboratory, a specialized facility designed to conduct large-scale genetic analyses.

In this way, the researchers measured the expression of every one of the worms' approximately 20,000 genes, to determine how that expression differed depending on food availability.

"We also did an experiment in which we took the starved worms and refed them, and took the fed worms and starved them, to see how rapid their response was to the changing conditions," Sternberg says.

The researchers found that the worms responded far more rapidly to being fed than being starved. Being fed also caused the activation of a far greater number of genes than did starvation. For example, three hours of feeding worm larvae that had previously been starved caused the activation of 381 genes, while starving formerly fed worm larvae for three hours caused the activation of only 56 genes.

In addition, the research revealed that as many genes are involved in the worms' response to nutrition as are involved in their overall development. Many of the genes that play a role in that nutritional response have to do with energy metabolism, and in changing the way the animals utilize and store energy.

"It looks like C. elegans is primed to respond faster to better conditions. It is optimistic," Sternberg says. "These worms live, most of the time, in scarcity. They are facing bad conditions--that is, no food--most of the time. Probably they've evolved to take advantage when times get better for a brief period. They grow and reproduce."

The worms' quick response to food appears to be controlled by a vital cellular protein called RNA Polymerase II (RNA Pol II), which is responsible for transcribing DNA into mRNA. In a separate experiment, Sternberg and his colleagues found that RNA Pol II accumulates on genes that respond rapidly to being fed, but in advance of that feeding.

"We speculate that this polymerase accumulation is part of the way in which they can respond so quickly. It's already engaged, ready to go, ready to send out the message. It's like having Paul Revere on the North Shore, ready to ride, when the food comes," Sternberg says.

"It is kind of interesting in hard economic times to think whether we can learn anything from this organism, in terms of being optimistic or pessimistic. Maybe the take-home message is that sometimes when you are faced with scarcity, you should still be optimistic."

Sternberg speculates that other nematodes, including the parasitic worms that cause elephantiasis in humans, and other lymphatic filarial diseases, may also go through similar transitions in nutrition as they transition from one host (say, a mosquito) to another (a human). Those transitions may be mediated by a similar accumulation of RNA Pol II on particular genes. Identifying those genes could provide potential targets for new types of therapeutic drugs.

More information: The paper, "RNA Pol II Accumulates at Promoters of Growth Genes During Developmental Arrest," was coauthored by Baugh, Sternberg, and John DeModena, a member of the biology research staff at Caltech.

Source: California Institute of Technology