In roundworms, fats tip the scales of fertility

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Caenorhabditis elegans. Credit: Wikipedia

Proper nutrition can unleash amazing powers, moms have always assured us, frequently citing Popeye the Sailor Man as evidence. Now, two University of Colorado Boulder scientists have confirmed just how potent some nutrients can be.

In findings published today in the journal *Cell*, postdoctoral fellow Hongyun Tang and Professor Min Han, both of CU Boulder's Department of Molecular, Cellular and Developmental Biology and the Howard Hughes Medical Institute, detail how fat levels in a tiny soil-dwelling roundworm (*C. elegans*) can tip the balance between whether the worm makes eggs or sperm.

Although the researchers discovered this phenomenon in worms, the research could have implications for future studies into human fertility and reproductive development.

Scientists have long recognized a connection between dietary fat and reproductive development in mammals, including humans.

"Studies in humans and rats have suggested that a high-fat diet is a major cause of early puberty in girls," said Han, the senior author of the paper. "It makes sense from an evolutionary standpoint that reproductive success would be coupled to food availability."

However, Han said, scientists understand surprisingly little about just how fat levels might be translated into fertility.

C. elegans comes in two sexes: males and hermaphrodites. Males produce sperm throughout their reproductive lives while hermaphrodites produce sperm only during a brief period, and later switch gears to making eggs.

Through a meticulous series of experiments, Tang homed in on one nutrient, a fatty acid called myristic acid, whose abundance, it turns out, worms can "monitor" using an enzyme called acyl-CoA synthase 4 (ACS-4). Fatty acids are chemical building blocks of dietary fats, so their level in a worm's body is one measure of the general nutritional quality of their food.

Tang found that the levels of certain fatty acids, including myristic acid, can influence the switch from sperm to egg production. When Tang depleted a particular myristic acid derivative from the germ cells in hermaphrodite worms by blocking the action of ACS-4, the worms never made the switch to making eggs.

Typically, a worm's sex-determination—in this case, making eggs or sperm—comes down to counting chromosomes. Hermaphrodites' cells have two sex chromosomes while males have only one. Tang, however, discovered that the worm's sex-determination system could also tap into information gathered by monitoring fatty acid levels.

But before the fatty acid can become tethered to the protein, it must be temporarily hitched to a molecule called CoA. ACS-4 is the enzyme that links myristic acid to CoA.

Tang found that the worms' sex-determination system can be overruled by the levels of myristoyl-CoA and myristoylated proteins. He determined that one component of the sex-determination system, a protein called MAP kinase, proved to be the link between the fatty acid monitoring and the switch from production of sperm to eggs.

This fatty-acid sensing phenomenon does not appear to be particular to hermaphroditic nematode species like *C. elegans*. When Tang partially blocked ACS-4 in females of a conventional male/female nematode species, many of the females made sperm instead of eggs.

The researchers call this newly-discovered ACS-mediated mechanism a "lipid sensor" and believe it could be a widespread strategy by which animals translate cues from the environment into physiological responses. The key proteins at work in the nematodes have highly similar counterparts in humans, suggesting that similar regulatory pathways may operate in people.

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