UT SOUTHWESTERN MEDICAL CENTER NEWS

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EMBARGOED UNTIL 11 A.M. CDT TUESDAY, APRIL 4, 2006

Worm's hunger response provides clue to eating disorders

DALLAS – April 4, 2006 – In research that may have implications for studying eating disorders in humans, a worm the size of a pinhead is helping researchers at UT Southwestern Medical Center unravel the mechanisms of hunger.

The researchers have found a series of biochemical reactions that control how the simple worm feeds, opening the way for further research into the complicated nature of hunger. Central to the research is a worm called *Caenorhabditis elegans*, which eats bacteria by contracting and relaxing a large muscle called the pharynx to suck in its prey. When it can't find food, *C. elegans* reacts by pumping the pharynx harder.

"Despite the prevalence of eating disorders from obesity to anorexia, the identity and mechanism of action of starvation signals are largely unknown," the researchers wrote in the paper, which will appear in the April issue of *Cell Metabolism.*

The study of the signaling pathways in feeding muscles suggests that feeding disorders may result from inappropriate behavioral responses to starvation signals, they wrote.

"Instead of being vague about what hunger is, we can be specific, at least in these cells in these particular animals," said Dr. Leon Avery, professor of molecular biology and senior author of the study. "There's been a lot of work on hunger and behavior, but hunger has not been well-defined at the molecular level."

The UT Southwestern researchers focused on receptor molecules on the surface of the *C. elegans*' pharynx. Receptors can be either activated or blocked, thus triggering or stopping reactions inside a cell, depending on what substance binds to them.

In this case, the scientists focused on muscarinic receptors, which regulate the speed of the heart, contraction of the pupil and other bodily functions. Their experiments followed biochemical reactions inside the pharynx muscle in both normal worms and mutants that were abnormally sensitive to starvation.

Activating the worms' muscarinic receptors triggered the same behavior and biochemical response that starvation did, showing that the receptor controlled the muscle's response to hunger.

When starved worms were placed back in the presence of food, their pharynxes showed a great increase in pumping rate compared to well-fed worms, suggesting that the muscle's biochemistry and physiology had altered to enhance the ingestion of food.

The findings may aid in understanding feeding in mammals, which also have muscarinic receptors, although mice and humans have five types, while *C. elegans* has only three.

When mice, for example, are genetically altered to lack the gene for one type of muscarinic receptor, they eat less and are skinnier than their normal counterparts.

One of the next research steps, Dr. Avery said, is to investigate what alerts the worm to its hunger. For example, do the nerve cells that respond to environmental cues and send the chemical signals that active the muscarinic receptors become more active during starvation, or does the pharynx somehow become more sensitive to those nerve signals?

The answers to these and other questions may eventually help guide research in mammals, Dr. Avery said.

Other UT Southwestern researchers involved in the study were Dr. Young-jai You, postdoctoral researcher in molecular biology and pharmacology, and Dr. Melanie Cobb, professor of pharmacology and dean of UT Southwestern Graduate School of Biomedical Sciences. Dr. Jeongho Kim, a visiting professor from Inha University in South Korea, also participated.

The work was supported by the National Institutes of Health and the Korea Research Foundation.

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