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Newly Discovered Gene Controls Social Eating Behavior

A small change in a single gene determines whether roundworms prefer to eat alone or with other worms. While that may seem of little consequence to humans, it turns out that this gene, called *npr-1*, is closely related to a human protein that binds to neuropeptide Y, a substance that helps regulate appetite and anxiety.

The newly discovered gene may be part of an ancient biological mechanism that arose millions of years ago, says Cornelia Bargmann, an HHMI investigator at the University of California, San Francisco (UCSF).

The investigators don't believe that a single gene will ultimately define the bread-breaking habits of humans, but they say their work invites further exploration of the extent to which genes influence behavior. "Although we believe that part of the natural variation in behavior within a species is due to genetic differences between individuals, the genes that contribute to that variability are largely unknown," says Bargmann.

The fact that a primary sociability trait has now been linked to a gene "is empowering," Bargmann says. "We may in fact be finding that genetic influences in behavior are traceable." Bargmann and colleague Mario de Bono, an HHMI associate at UCSF published their study in the September 4, 1998, issue of the journal *Cell*.

Bargmann and de Bono chose the tiny, transparent nematode *C. elegans* to study natural variation in behavior because this worm has a simple nervous system, well-understood genetics, and there are many wild strains available.

"By studying these receptors in worms, we hope to understand how the same molecules function in mammals," says de Bono.

Observing that some naturally occurring worm strains clump together when feeding while others forage alone led Bargmann and de Bono to look for a gene that differed between the two types of worms. The investigators found that one form of the gene, *npr-1 215F*, is found exclusively in what Bargmann and de Bono call social worm strains, while another form of the gene, *npr-1 215V*, occurs only in solitary feeders.

By adding the "solitary" form of the gene to the "social" worms, the investigators changed the worms from social feeders to solitary feeders.

Further study showed that *npr-1* codes for a nerve cell receptor similar to a ubiquitous protein receptor found in human brains. Neuropeptide Y, the protein that binds to this receptor, is part of a family of neuropeptides which regulate a wide range of behaviors and biological functions in mammals, including feeding, obesity, emotional state, memory blood pressure and digestion. These proteins "don't affect the ability, but rather affect the probability" that a behavior will occur, says Bargmann.

This discovery may offer clinical benefits in the future, says de Bono. Regulation of neuropeptide Y receptors may prove helpful in controlling clinical conditions, he says. "For example, we may be able to use the worm to predict how certain genes regulate blood pressure or feeding behavior in mammals," says de Bono. "We are excited because this information could be very useful if similar mechanisms operate in worms and in humans."