Single gene invites worms to dinner party

While some people relish a solitary meal out, many dread the prospect of eating alone in a restaurant.

A similar social dichotomy exists among certain worms. Faced with a feast of bacteria, some strains of the nematode *Caenorhabditis elegans* prefer to munch their microbial meals without companions, while members of other strains swarm into writhing dinner parties. Two San Francisco researchers have now found that the only difference between the solitary and social strains is a small change in a single gene.

The newly identified worm gene resembles several human genes, say Mario de Bono and Cornelia I. Bargmann of the Howard Hughes Medical Institute at the University of California, San Francisco. They, however, caution against extrapolating from the feeding habits of worms to complex human behavior.

"I don't think this is the social gene that determines whether you hang out with people at parties," says Bargmann.

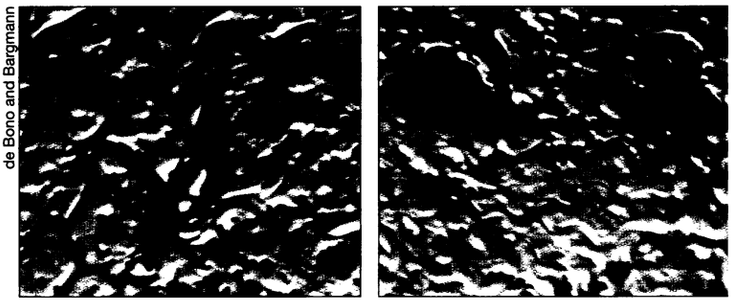
Still, the human genes similar to the nematode gene are implicated in eating behavior, suggesting that the worm may offer insight into more complex animals. "We're now getting at genes that influence natural variation [in behavior]. It was thought for many years that was impossible," notes Marla B. Sokolowski of York University in Toronto, who studies the genetics of fruit fly feeding behavior (SN: 8/23/97, p. 127). The hope, says Sokolowski, is that scientists will "pull out new components of a pathway involved in the regulation of feeding that will be relevant to mammals."

Researchers working with strains of *C. elegans* from around the world have long recognized a split in nematode eating behavior. When placed on a dish covered with bacteria, members of some strains disperse to forage alone. Other strains form clumps of up to several hundred worms.

De Bono and Bargmann tracked down the gene behind these differences by examining examples of a solitary strain of *C. elegans* that had become social after exposure to a mutation-causing chemical. The disabling of a single gene, they report in the Sept. 4 CELL, brings about the conversion.

The gene, called *npr-1*, resembles human genes for proteins on the surface of brain cells that recognize neuropeptide Y, the most potent eating stimulant yet identified in mammals (SN: 7/27/96, p. 63). The investigators found that a single variation in *npr-1*'s DNA sequence accounts for the differences between natural solitary and social strains. All the solitary strains had a *npr-1* that encoded the amino acid valine in one part of the receptor, but the social strains' version substituted phenylalanine.

How such a subtle alteration in a brain cell receptor explains the two strains' distinctive behaviors remains unclear, although it may affect how a worm senses or responds to food or other nematodes. Bargmann notes that the receptor's gene doesn't completely determine worm social behavior. Solitary worms do swarm under certain conditions, she says, and members of social strains will strike out on their own when no food is around. —*J. Travis*



de Bono and Bargmann

Solitary (left) and social (right) worms dine on microbes.

A protein is pivotal in prostate cancer

Prostate cancer can be a Jekyll-and-Hyde disease. Some cases progress slowly, and some aggressively. Cancers initially contained by treatment can later become fierce and deadly.

Scientists at Memorial Sloan-Kettering Cancer Center in New York now link the dual identity of prostate cancer to a protein encoded by the *p27* gene. Degradation of this cancer-suppressing protein has been implicated in other malignancies, and the new research confirms that rampant destruction of p27 protein occurs commonly in the most aggressive prostate cancers.

The study, described in the Sept. 2 JOURNAL OF THE NATIONAL CANCER INSTITUTE, also suggests that benign prostatic hyperplasia (BPH), an enlargement of the prostate in older men, isn't necessarily a precursor of cancer, as often feared.

Normally functioning cells make p27 protein nonstop. Instructions from the *p27* gene are carried by messenger RNA to the molecular machinery that makes the protein. Enzymes regularly chop up the p27, leaving just enough to keep the cell from dividing. When it comes time for cell division, the enzymes destroy all available p27 protein. More is made an instant later.

"We don't know the specific enzymes of p27 degradation," but their function seems clear, says Michele Pagano, a cell biologist at New York University and the Kaplan Comprehensive Cancer Center in New York. "You need specific traces of [p27 and other] proteins, but you also need to get rid of them fast."

The new study indicates that in aggressive prostate cancer, "the tumor is getting rid of [p27 protein] all the time," allowing unchecked cell growth, says Massimo Loda, a pathologist at the Dana-Farber Cancer Institute in Boston.

To explore the protein's role, researchers examined samples of prostate tissue from 4 healthy men, 14 BPH patients, and 130 men whose cancerous prostates had been removed—including 32 in whom the cancer had spread beyond the prostate. Of this last group, 78 percent had unusually depressed or undetectable concentrations of p27. Among the other cancer patients, 64 percent had low or undetectable levels of p27. The healthy subjects and 32 percent of all the cancer patients had normal amounts of p27 in their prostate tissue.

The results suggest that prostate cancer can develop along two distinct pathways—one in which a loss of the protein p27 allows unbridled cell proliferation and another that circumvents the growth-suppressing effects of p27—says study coauthor Carlos Cordon-Cardo, a pathologist and cell biologist at Memorial Sloan-Kettering.

"We're not saying [degradation of] p27 is *the* cause of prostate cancer," Cordon-Cardo cautions. "Probably, there are other mechanisms there already."

The researchers note that the 14 patients who had BPH, a noncancerous proliferation of muscle cells in the prostate, also lacked p27 protein—but not because enzymes were chopping it up. Instead, the BPH patients had little or no *p27* messenger RNA.

None had cancer, indicating that a simple lack of the protein may result in this benign cell proliferation but not malignancy. "These two conditions were very different," which suggests BPH isn't a precursor for cancer, says Cordon-Cardo.

The cancer danger seems to arise when a person's cells make p27 but then destroy it, he says, rather than when there are mutations in its gene. A prostate cancer patient's p27 concentrations may tip off doctors as to the potential severity of the cancer, he says, better enabling them to decide on treatment. —*N. Seppa*