Study suggests link between tumor suppressors and starvation survival

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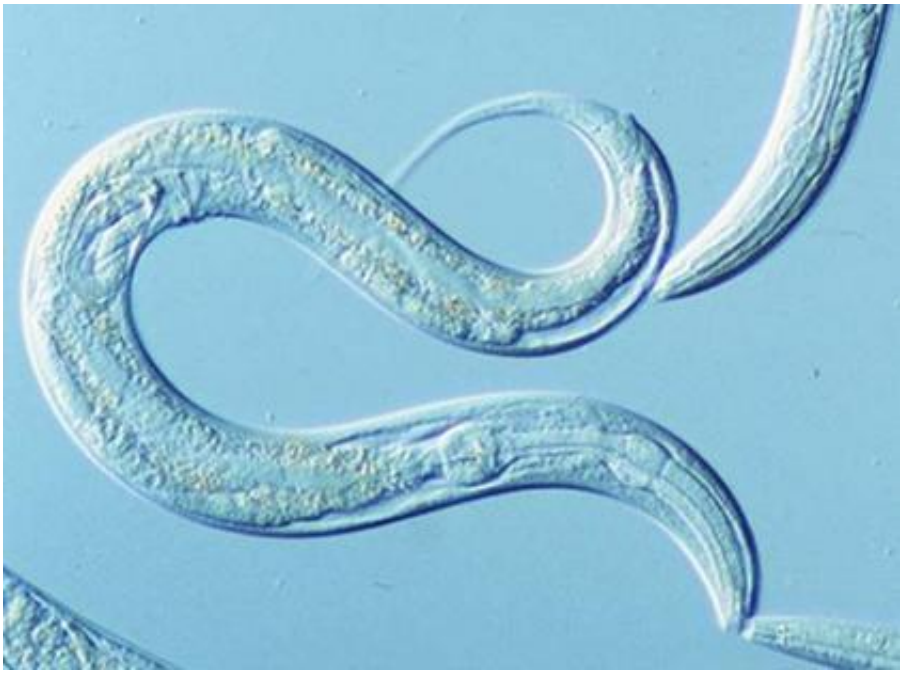

A tumor supressor gene found in the common laboratory nematode, C. elegans, has been shown to not only shut down cancerous cell division but also to fend off stress, according to a new University of Colorado Boulder study. Credit: NIH

A particular tumor suppressor gene that fights cancer cells does more than clamp down on unabated cell division—the hallmark of the disease—it also can help make cells more fit by allowing them to fend off stress, says a University of Colorado Boulder study.

CU-Boulder Professor Min Han said the research team was interested in how a common tumor suppressor gene known as Retinoblastoma 1, or Rb, behaved under conditions of starvation. The question is important, said Han, because it may help researchers understand why many cancer cells are more susceptible to starvation or fasting than ordinary cells.

Han and his team studied a popular lab organism called C. elegans, a translucent nematode smaller than an eyelash. Many of the C. elegans genes have similar, corresponding human genes called homologs, and almost all cellular mechanisms found in the nematodes also are found in mammals, including humans, he said. The team charted changes in the physiology of newly hatched C. elegans in the absence of food to look at the corresponding stress response.

"We found the tumor suppressor Rb is a critical regulator of the starvation response," said Han, who also is a Howard Hughes Medical Investigator. "Rb is known for doing more than just suppressing cell division associated with cancer—it carries out a host of other cellular tasks including regulating development. The new findings by our group and research by other groups suggest organisms survive longer when they encounter starvation by regulating the expression of a large number of genes."

A paper on the subject was published online May 9 in *Current Biology*, a publication of Cell Press. The co-authors on the study, Mingxue Cui, Max Cohen and Cindy Teng, are all researchers associated with both CU-Boulder and HHMI. The study was funded by HHMI and the National Institutes of Health.

As part of the study, the researchers monitored the two- to three-week survival time of hundreds of C. elegans hatchlings in an environment with no food, which caused immediate "developmental arrest," said Han, a professor in CU-Boulder's molecular, cellular and developmental

biology department. "The survival time of the young nematodes is dramatically shorter when the Rb gene is mutated, which causes changes in the activities of multiple cell signaling pathways."

The study suggests that Rb plays a critical role in maintaining a starvation-induced "transcriptome," which is the transcription of DNA to corresponding bits of RNA that allow researchers to pinpoint when and where each gene is turned on or off in the cells, he said. Under starved conditions, for example, Rb represses some responses induced by other physical stressors like pathogens and toxins.

Han said the Rb gene is mutated in a large percentage of human cancers. Hundreds of mutations in the RB gene have been identified in people with retinoblastoma, a rare type of eye cancer that usually strikes young children.

"Altogether, these findings identify Rb as a critical regulator of the starvation response and suggest a link between functions of tumor suppressors and starvation survival," the team wrote in Current Biology. "These results may provide mechanistic insights into why cancer cells are often hypersensitive to starvation treatment."

Provided by University of Colorado at Boulder