Genes that both extend life and protect against cancer identified

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A person is 100 times more likely to get cancer at age 65 than at age 35. But new research reported today in the journal *Nature Genetics* identifies naturally occurring processes that allow many genes to both slow aging and protect against cancer in the much-studied C. elegans roundworm.

Many of the worm genes have counterparts in humans, suggesting that new drugs may some day ensure a long, cancer-free life. The new research and a related study the scientists reported in “Science” last year indicate that cellular changes leading to longevity antagonize tumor cell growth.

The studies are by scientists at the University of California, San Francisco, who say the research also underscores the deep evolutionary connection between lifespan and cancer.

The worms, known formally as Caenorhabditis elegans, were the stars of a startling 1993 discovery by UCSF biologist Cynthia Kenyon, PhD. She found then that a change in just one gene, called daf-2, doubled the worms’ lifespan. This finding led to the understanding that lifespan is regulated by genes and is therefore changeable, rather than the inevitable result of the body’s breakdown. The discovery in worms has been confirmed in other animals including mice.

The new research by Kenyon and graduate student Julie Pinkston is reported in the advanced online edition of the journal.

Kenyon is the American Cancer Society Professor and director of the Hillblom Center for the Biology of Aging at UCSF.

“This is very exciting,” Kenyon said. “There is a widely held view that any mechanism that slows aging would probably stimulate tumor growth. But we found many genes that increase lifespan, but slow tumor growth. Humans have versions of many of these genes, so this work may lead to treatments that keep us youthful and cancer-free much longer than normal.”

Since her early finding that the gene daf-2 and another gene known as daf-16 regulate lifespan, Kenyon’s research team has hoped to identify the genes that they in turn affect -- those that more directly affect aging and tumor growth.

“Now we are really getting there,” Kenyon said.

The gene daf-2 codes for a receptor for insulin and also for an insulin-like protein that promotes growth. It influences daf-16, which makes a so-called transcription factor – a protein that determines when and where hundreds of other genes are turned on. The focus of the new study was to identify specific genes regulated by daf-16 which affect cancer and/or lifespan.

The scientists used an established tumor model in the worms. Then, starting with a list of 734 genes known to be targets of daf-16, they identified 29 genes that either promote or suppress tumor cell growth. They did this using several techniques, including RNA interference or RNAi, a powerful tool that allows scientists to control the expression of just one kind of gene at a time.

About half of the genes stimulated tumor growth and half suppressed it, they found. Strikingly, about half of these genes also affect lifespan in

animals that do not have tumors, further strengthening the model Kenyon and others have conceived in which the insulin receptor, daf-2, works in concert with the transcription factor daf-16 to link longevity and tumor resistance. The “downstream” genes appear to act in a cumulative way, they found.

The genes that stimulated tumor growth also accelerated aging itself, and the genes that prevented tumor growth slowed down the aging process and extended lifespan. These findings greatly strengthen the view that the controls of lifespan and cancer have deep, common roots, Kenyon and Pinkston conclude.

Source: University of California - San Francisco