Blame our evolutionary risk of cancer on body mass

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A key enzyme that cuts short our cellular lifespan in an effort to thwart cancer has now been linked to body mass. Until now, scientists believed that our relatively long lifespans controlled the expression of telomerase--an enzyme that can lengthen the lives of cells, but can also increase the rate of cancer.

Vera Gorbunova, assistant professor of biology at the University of Rochester, conducted a first-of-its-kind study to discover why some animals express telomerase while others, like humans, don't. The findings are reported in today's issue of *Aging Cell*.

"Mice express telomerase in all their cells, which helps them heal dramatically fast," says Gorbunova. "Skin lesions heal much faster in mice, and after surgery a mouse's recovery time is far shorter than a human's. It would be nice to have that healing power, but the flip side of it is runaway cell reproduction--cancer."

Up until now, scientists assumed that mice could afford to express telomerase, and thereby benefit from its curative powers, because their natural risk of developing cancer is low--they simply die before there's much likelihood of one of their cells becoming cancerous.

"Most people don't know that if you put mice in a cage so the cat can't eat them, 90 percent of them will die of cancer," says Gorbunova.

Evolution, it seems, has determined which species are allowed to express

telomerase in their somatic cells in order to maintain a delicate balance between cells that live long, and cells that become cancerous. But while most scientists believed an organism's lifespan determined whether it was at a higher risk of cancer, Gorbunova has revealed evidence that it is not our long lifespan that puts us at risk, but our much-heavier-than-a-mouse body mass.

The tips of chromosomes, called telomeres, shorten every time a cell divides. After about 60 divisions, the telomeres are eroded away to the point that the cell stops dividing. Telomerase rebuilds those tips, so animals that express it, like mice, have cells that can reproduce more extensively and thus heal better. Cancer cells, however, are those cells that constantly reproduce unchecked, and so evolution has shut off the expression of telomerase in human somatic cells, presumably because the threat of cancer outweighs the benefits of quick-healing.

But no one has looked into why mice express telomerase and humans don't. In fact, telomerase activity has been barely catalogued in the animal kingdom. Gorbunova decided to take on the question by creating a unique test. She investigated 15 rodents from across the globe to determine what level of telomerase activity each species expressed, to see if there were some correlation she could find.

The species ranged from tiny field mice to the 100-pound capybara from Brazil. Lifespans ranged from three years for the mice, to 23 or more for common backyard squirrels.

Acquiring specimens of these animals from around the world proved to be an unusual task.

"At one point I was woken up at two in the morning by a guy on a cell phone hunting pest beavers in Montezuma," says Gorbunova. "I'm still trying to wake up and this voice says, 'I hear you're looking for beavers.'

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For over a year, Gorbunova collected deceased rodents from around the world and had them shipped to her lab in chilled containers. She analyzed their tissues to determine if the telomerase was fully active in them, as it was in mice, or suppressed, as it is in humans. Rodents are close to each other on the evolutionary tree and so if there were a pattern to the telomerase expression, she should be able to spot it there.

To her surprise, she found no correlation between telomerase and longevity. The great monkey wrench in that theory was the common gray squirrel, which lives an amazing two decades, yet also expresses telomerase in great quantity. Evolution clearly didn't see long life in a squirrel to be an increased risk for cancer. Body mass, however, showed a clear correlation across the 15 species. The capybara, nearly the size of a grown human, was not expressing telomerase, suggesting evolution was willing to forgo the benefits in order to reign in cancer.

The results cannot be directly related to humans, but Gorbunova set up the study to produce very strong across-the-board indicators. It's clear that evolution has found that the length of time an organism is alive has little effect on how likely some of its cells might mutate into cancer. Instead, simply having more cells in your body does raise the specter of cancer--and does so enough that the benefits of telomerase expression, such as fast healing, weren't worth the cancer risk.

Gorbunova points out that these findings raise another, perhaps far more important question: What, then, does this mean for animals that are far larger than humans? If a 160-pound human must give up telomerase to thwart cancer, then what does a 250,000-pound whale have to do to keep its risk of cancer at bay? "It may be that whales have a cancer suppressant that we've never considered," says Gorbunova. "I'd like to find out what kind of telomerase expression they have, and find out what

else they use to combat cancer."

As for the tiny mice: "They don't have to worry about cancer," she says. "They're probably all praying for an anti-cat gene."

Source: University of Rochester