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News: Health,Genetics,Animals

A resurrected gene may protect elephants from cancer

LIF6 instructs damaged cells to self-destruct before the disease has a chance to take hold

By Aimee Cunningham 2:23pm, August 14, 2018

SECRET WEAPON Elephants have some unique defenses against cancer, including a once-dormant gene that plays a role in killing damaged cells before they have a chance to turn cancerous.

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Elephants rarely succumb to cancer. That's surprising given how large the animals grow and how long they can live, which should provide more opportunities for cells to morph into cancer cells. A newly described gene that was brought back from the dead may take part in protecting the animals from the disease.

A deep dive into elephants' evolutionary history revealed a defunct gene called *LIF6* that was somehow resurrected roughly 59 million years ago, around the time that elephants' ancestors began to develop larger body sizes. Found only in elephants and their ancestral kin, *LIF6* is triggered by another gene, *TP53*, to put cells out of commission at the first sign of damage before they turn cancerous, researchers report online August 14 in *Cell Reports*.

Previous research on elephants' cancer-fighting powers focused on *TP53*, which most animals have. It was known that the gene makes a protein that detects cellular DNA damage and signals for a cell to repair itself or self-destruct, which also helps stop damaged cells from turning into cancer cells. In 2015, researchers found that elephants have 20 *TP53* copies, compared with just one for humans and other mammals (*SN: 11/14/15, p. 5*).

"What's really fascinating to me about the elephant is that it's not one mechanism" that underpins cancer resistance, says Lisa Abegglen, a cell biologist at the University of Utah School of Medicine in Salt Lake City, who was part of the 2015 discovery.

That study, which examined autopsy data from the San Diego Zoo and a database of nearly 650 elephant deaths, also found that just 4.8 percent of the animals die of cancer. For humans, that number ranges from 11 to 25 percent. Understanding the different ways that elephants resist cancer could provide insights into treating the disease in people.

In experiments with elephant connective tissue cells in a dish, evolutionary biologist Vincent Lynch at the University of Chicago and colleagues used a chemical to damage the cells' DNA. The damage made *LIF6* eight times as active in those cells compared with ones not treated with the chemical. And nearly all of *LIF6*'s activity was wiped out when researchers blocked *TP53* from making its protein.

Learning how elephants and other animals resist cancer could help solve a riddle called Peto's paradox, which describes how the occurrence of cancer across species does not seem to increase with size and life span. Take humans and mice: Humans have 1,000 times as many cells and live 30 times as long as mice, so human cells have more chances to develop DNA errors and damage that might progress to cancer. But epidemiologist Richard Peto observed in the mid-1970s that humans and mice have a similar lifetime risk of developing cancer. Therefore, longer-living, larger-bodied animals must have developed more mechanisms for nipping cancerous changes in the bud than shorter-living, smaller-bodied animals.

More work is needed to figure out how *TP53* and *LIF6* potentially help elephants fight cancer, Abegglen says. But the animals likely "wouldn't be so large and long-lived if these changes in genes that are unique to the elephant hadn't occurred."

Citations

J.M. Vazquez et al. A zombie LIF gene in elephants is upregulated by TP53 to induce apoptosis in response to DNA damage. *Cell Reports*. Published online August 14, 2018. doi:10.1016/j.celrep.2018.07.042.

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Further Reading

M. Rosen. Elephant's cancer-protection secret may be in the genes. *Science News*. Vol. 188, November 14, 2015, p. 5.