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Week of October 26, 2015 – Elephants: The Key to a Cancer Cure

It turns out that just 4.8 percent of known elephant deaths are related to cancer. For humans, cancer-related deaths are much more common; between 11 and 25 percent. The elephant's low cancer rate is particularly interesting because, all things being equal, elephants should get more cancer than we do. Elephants have about 100 times as many cells as humans, and they have a lengthy life span, about 70 years. That gives a lot of cells a lot of opportunity to mutate and turn malignant.

For decades scientists have wondered why elephants and large mammals are generally not more prone to cancer than smaller mammals. The question even has a name: Peto's paradox (named after epidemiologist, Sir Richard Peto for his work in the 1970's and 1980's). But new research may shed light on pachyderms' cancer-fighting abilities.

In a recently paper published in the Journal of the American Medical Association, a team of scientists learned that African elephants have 20 chromosome copies (and therefore 40 alleles) of a gene called TP53, sometimes called the "guardian of the genome." TP53 is known for its ability to create a protein that suppresses tumors. Humans have just one copy (two alleles) of this gene.

Whoa, OK, let's slow down here and go over a little biology. First of all, an allele is one of two or more versions of a gene (as a matter of fact, the word "allele" is a short form of *allelomorph*, meaning "other form" which comes from the Greek prefix, *allel*, meaning "each other."). Each person inherits two alleles for each gene; one from each parent. If the two alleles are the same, the individual is homozygous for that gene. If the alleles are different, the individual is heterozygous. Though the term "allele" was originally used to describe variation among genes, it now also refers to variation among non-coding DNA sequences. And let's remember that the basic unit of heredity consists of a segment of DNA arranged in a linear manner along a chromosome; and chromosomes are thread-like structures located inside the nucleus of animal and plant cells. Each chromosome is made of protein and a single molecule DNA. DNA contains the specific instructions that make each type of living creature unique.

So elephants possess a greater ability to produce the TP53 gene. Elephants also detect damaged cells preemptively, which they then repair or kill. Thus, it appears that they may have a *robust* mechanism for killing damaged cells that are at risk for becoming cancerous.

This ground-breaking study was conducted by a team of scientists from the University of Utah and Arizona State University. White blood cells (infection-fighting cells) from elephants were extracted and had their DNA damaged. This can commonly trigger cancer, whereby the cells with p53 reacted predictably and destroyed themselves. "It's as if the elephants said, 'It's so important that we don't get cancer, we're going to kill this cell and start over fresh.'" This according to the study's author and a pediatric oncologist at the University of Utah School of Medicine, Joshua Schiffman.

The University researchers attest that if a damaged cell is killed, it's gone, and it can't turn into cancer. This may be more effective of an approach to cancer prevention than trying to stop a mutated cell from dividing and not being able to completely repair itself.



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Without the genetic cancer-fighting ability, elephants would be long gone. Cancer researchers acknowledge that by all logical reasoning, elephants, throughout the ages, should have developed cancer at such a prolific rate that, in fact, they should be extinct by now due to such a high risk for cancer. The recent study that identified the TP53 gene suggests that by the ability of elephants to manufacture p53 is nature's way of keeping this species alive. While there are other contributing factors that make humans more at risk of getting cancer, experts said, the study provides insight on treatment. As Schiffman states, "Nature has already figured out how to prevent cancer. It's up to us to learn how different animals tackle the problem so we can adapt those strategies to prevent cancer in people."

Part of the team's research included studying patients who have Li-Fraumeni Syndrome, a rare hereditary disorder that increases the risk of developing certain cancers, like breast and a kind of bone cancer called osteosarcoma. The researchers compared the cells of people with Li-Fraumeni Syndrome, healthy, cancer-free people, and elephants. Elephants killed pre-cancerous cells at a rate five times greater than people with the syndrome.

Indeed, this surprised researchers and now believe that by continuing to study elephants, new developments in human cancer treatments could be not far off. The University research team members have stated a very interesting theory regarding humans and their lifestyles and the susceptibility to cancer. That is, there is a line of thinking that humans develop cancer so frequently because they do not live the lifestyles they were evolved to live. From the lack of exercise to eating unhealthy foods, modern humans have put themselves on a somewhat unnatural track.

After presenting some of his early findings at a conference, Schiffman was approached by another unlikely collaborator: the circus! The Ringling Brothers Center for Elephant Conservation reached out to Schiffman to see if he would like to analyze the samples of their herd of Asian elephants, the largest in North America. Schiffman had previously studied blood samples from African elephants and this gave him the opportunity to see if this cancer-fighting genetic capability extended beyond the sample group he was studying. The answer was yes, and now the circus's parent company, Feld Entertainment has announced a new funding effort to support this continued elephant research.

The circus has also pledged to donate \$10,000 to the local children's hospital or treatment center in the next 50 cities it tours through. The Ringling Bros. Children's Fund will then match each donation with an additional \$10,000 to the Primary Children's Hospital Pediatric Cancer Research Program. The partnership is something of a win-win between the join University research team and the circus. The exposure surrounding this cancer research also underscores the importance of elephant conservation.

So what's next? Maybe, through the elephant, we may be approaching the end of our long road to finding an effective treatment and even a possible prevention of cancer in our lifetime.

Always forgive your enemies - nothing annoys them so much.

Oscar Wild

