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Researchers complete the largest compilation of cancer prevalence across vertebrates

For all its pervasiveness and the efforts to study it, cancer is still somewhat of a mystery. Why do some animals get it at a higher rate than others? This is the question at the heart of Peto's paradox, the observation that large animals, by virtue of their number of cells, are statistically more likely than smaller animals to develop and accumulate genetic mutations that lead to cancer, yet they don't. In fact, some large animals, including whales and elephants, get much less cancer than expected for an animal of its body size and number of cells.

UC Santa Barbara anthropologist Amy Boddy and her collaborators are working to gain insight on this and other cancer mysteries. In the culmination of a decade-long effort, they have completed a compilation of cancer prevalence across 292 species of vertebrates, including amphibians, reptiles, birds and mammals.

This broad look at cancer prevalence — the largest study of its kind — could allow researchers opportunities to investigate the strategies of species with exceptional cancer resistance. Among the least likely to develop tumors that could lead to cancer? The common porpoise and the black-footed penguin. Among the most likely? Ferrets and opossums. But these are among the outliers, the most extreme cases.

“One thing that became really clear once we started gathering the data is that everything gets cancer,” said Boddy, a biologist, evolutionary theorist and co-author of the new paper, published in the journal Cancer Discovery. “It’s just something about being a multicellular organism. No one’s completely protected.”

Indeed, according to the paper, cancer “is a problem of multicellularity.” The emergence of multicellular life opened the doors to complexity, with different cell types coexisting and communicating with each other. But with this complexity comes some vulnerability in the form of genetic mutations that cumulatively can lead to the uncontrolled tissue growth that is the hallmark of cancer.

Having such a broad dataset allowed the researchers to control for various factors across species. In one case, they encountered a slight limitation to Peto’s paradox: When controlling for gestation length, adult weight did correlate with cancer prevalence, an association that was not observable in previous, smaller studies of cancer prevalence. Boddy is careful to point out that the effect is “very small,” however, and not enough to disprove the paradox.

Meanwhile, in favor of Peto’s paradox, animals with longer gestation times, which is associated with bigger bodies, tend to get fewer cancers. The researchers hypothesize that vertebrates that have longer gestation times are also investing more resources toward avoiding mutations.

“Bigger, long-lived species invest more in somatic maintenance,” Boddy said. “I’d expect them to be better at defending against cancer, because they have to, in order to grow big and live long. It’s not really a paradox from an evolutionary point of view.”

How the cancer-avoiders manage to evade the disease most likely comes down to the strategies individual species have developed over the course of their evolutionary history.

“Cancer is quite evolutionarily old, and is a constant selective pressure,” Boddy said. Animals and cancer have been evolving against each other for a long time. As animals developed into distinct species, she explained, they’ve had to undergo different genetic trade-offs and employ different strategies. One well known strategy is that of elephants, who have 20 copies of P53, a tumor suppressor gene. Other strategies may involve lower somatic mutation rates, so these mutations are slower to accumulate and develop into cancer.

“That’s also why I think we don’t find a general pattern across vertebrates, because each species has a unique story of why and how they need to defend against cancer,” Boddy said.

Another benefit of this data is that it could broaden the options for cancer research, she added. Studies tend to focus on rodent models, however animals that get cancer more spontaneously, or tend to get different types, might provide better data for researchers of cancer and rare diseases.

The next step for The Boddy Lab is to examine specific types of cancer across species. “Cancer is not a single disease,” she said. “It’s like 300 different diseases.” They’ll be looking to see, for example, if other members of the primate family get the same types of cancers that humans get. They’re also curious about the mechanisms that underlie the development of cancer in species that have a higher prevalence for it.

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