Whales are well protected against cancer (and that's good news for research)

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According to a recent study, the exceptional longevity (200 years) of the bowhead whale is due to the presence of a very efficient DNA repair mechanism that prevents the development of several diseases, in particular cancer.

Since every cell of an animal has the potential to become cancerous during its lifetime, there should in theory be a higher incidence of cancer in large species (elephants and whales, for example) that contain a very large number of cells, compared to smaller species (e.g. mice) which have far fewer. In reality, this is absolutely not what is observed, because there is no correlation between the size of an animal and its risk of developing cancer.

This phenomenon, known as Peto's paradox, therefore suggests that the evolution of large animals took place in parallel with the acquisition of protective mechanisms against cancer.

The study of these cancer-resistant animals therefore represents a very promising approach to identifying new anti-cancer therapeutic targets (1).

BICENTENARY WHALES

The bowhead whale (*Balaena mysticetus*), which lives in Arctic waters, is in this sense an excellent subject of study.

This gigantic animal, which can reach 18 meters in length and weigh up to about 100 tons (100,000 kilos), is very resistant to all diseases, including cancer, and can live in some cases more than 200 years, making it the longest-lived mammal on the planet.

A study recently submitted for pre-publication provides interesting information on the mechanisms involved in the resistance of these animals to cancer (2).

In this study, researchers examined the ability of bowhead whale cells to repair spontaneously occurring breaks in DNA that can cause mutations supporting the development of cancer. They observed that, compared to cells from other species (human, mouse, cow), those from the bowhead whale were much more efficient in repairing this damage and were able to regenerate with great fidelity the intact DNA structure.

The results of the study suggest that this effective restoration would be made possible by the presence of very high amounts of two proteins (CIRBP and RPA2) which increase the efficiency of the mechanisms responsible for DNA repair.

REPAIR RATHER THAN DISPOSAL

This anticancer defense based on repairing damaged DNA in bowhead whales is very different from that identified in other large animals. In elephants, for example, the rarity of cancers in these animals has been

shown to be caused by the presence of additional copies of a tumor suppressor gene (p53) (3).

In the presence of DNA lesions, these tumor suppressors activate a cell suicide program (apoptosis) which accelerates the elimination of damaged cells.

Without judging the superiority of any one of these strategies (each evolved in a specific context), the important point is that there are many ways in nature to reduce the development of cancer and that one can use these mechanisms as a source of inspiration to develop new anti-cancer treatments for humans.

(1) Caulin AF and Maley CC. Peto's Paradox : evolution's prescription for cancer prevention. Trends Ecol. Evol. 2011 ; 26 : 175-182.

(2) Firsanov D et al. DNA repair and anti-cancer mechanisms in the longest-living mammal : the bowhead whale. bioRxiv.org (deposited May 8th 2023).

(3) Abegglen LM et al. Potential mechanisms for cancer resistance in elephants and comparative cellular response to DNA damage in humans. JAMA 2015 ; 314 :1850-60.

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