Review of: "Is creeping abandon of human cancer defences evolutionarily favoured?"

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Potential competing interests: No potential competing interests to declare.

Different species indeed exhibit variations in their susceptibility to cancer. Some species, such as elephants and whales, have lower cancer rates relative to their body size and longer lifespans. This phenomenon is known as "Peto's paradox".

Researchers are actively studying Peto's paradox to better understand the mechanisms underlying the variations in cancer susceptibility among different species. It is believed that evolutionary adaptations, genetic factors, and specific biological characteristics must contribute to the lower cancer incidence in different species.

For example, elephants possess multiple copies of a tumor-suppressor gene called p53, which helps prevent the formation and growth of tumors. Additionally, some species have efficient DNA repair mechanisms or enhanced immune systems that can detect and eliminate cancerous cells more effectively.

The question of why humans may have a higher cancer risk compared to other closely related species, such as chimpanzees, is (as well stated here) unknown. Nevertheless, several hypotheses have been proposed to explain which evolutionary factors have led to a decrease in anti-cancer defenses in humans:

1. Trade-offs and evolutionary constraints: evolution involves trade-offs, where the development of certain traits or adaptations may come at the expense of others. It is possible that the unique characteristics and evolutionary pressures that shaped humans, such as increased brain size and energy demands, may have constrained the allocation of resources towards anti-cancer defenses. In other words, evolution may have prioritized other advantageous traits over enhanced cancer protection.
2. Genetic factors and mutations: genetic changes, including mutations, may have influenced the anti-cancer defenses in humans. Alterations in key genes involved in DNA repair, cell cycle regulation, or tumor suppression mechanisms could have occurred during human evolution, leading to a higher susceptibility to cancer.
3. Environmental factors and lifestyle changes: the shift in human lifestyle and environmental exposures over the course of evolution could have contributed to increased cancer risk. Factors such as dietary changes, exposure to carcinogens (including tobacco, pollutants, and industrial chemicals), and sedentary lifestyles may have played a role in altering human susceptibility to cancer.
4. Evolutionary trade-offs related to reproduction: one hypothesis suggests that the evolution of human reproductive strategies, including the extended female lifespan beyond reproductive age, could have influenced cancer susceptibility. The decline in selective pressure against late-onset diseases like cancer after reproductive age may

have allowed genetic variants that increase cancer risk to persist in the population.

Said all this, I suggest to considerer these comments to better present the points on setting the hypothesis (point 2) and the hypothesis (point 3).

It is import to note that these hypotheses are not mutually exclusive, and multiple factors likely interacted and shaped the evolution of cancer susceptibility in humans. Consequently, this obvious fact should be taken into consideration when proposing an experimental approach (point 4).