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

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Potential competing interests: No potential competing interests to declare.

The hypothesis is interesting, but poorly supported. It stems from the idea that cancer is determined by genetic or epigenetic mutations that occur randomly, although facilitated by environmental factors. If so, Peto's paradox should not exist: species with larger body mass would have more cancers. To explain this paradox, retaining the idea that cancer is due to random mutations, one needs to introduce the concept that the species which supposedly have lower cancer rates, and particularly those of larger size, should have increased anti-cancer immunity. These assumptions are difficult to prove.

However, we have evidence that cancer, or, better tumors, although rare, occur in all forms of multicellular life, and tumors are documented in the paleontological record, even among large dinosaurs. Tumors are documented also in the human paleontological record, although very rarely. In the historical record, cancer is documented since the dawn of civilization, but, again, seems to have been rare. A dramatic increase in cancer incidence, not necessarily reflected in increased mortality due to progresses in prevention and therapy at least for some forms, has occurred during the last century. This dramatic increase in cancer rates parallels the current explosion of the human population across the globe, and the technologies that allow increased inter-human contact, beyond the traditional limits of tribes or villages, or even cities, regions and continents.

This would fit the idea that cancer is a communicable disease, arising long after exposure to causative agent(s), a delay which would blur the picture and introduce confounding factors. The mutations would have nothing to do with the etiology of cancer, although they would facilitate disease development, or even be required for disease, as is the case for all communicable diseases that arise shortly after exposure and are therefore easily recognized as such (see for instance Covid-19).

The concepts expressed above would require a global reconsideration of the cancer problem, whose conceptualization has been heavily distorted by the tremendous increase in genetic technologies, which highlighted peculiarities not essential to the disease. Such peculiarities attracted widespread attention and were erroneously interpreted as pathogenetic (i.e. causal) factors.

The hypothesis of a creeping abandon of immunity during human evolution is an attempt to explain Peto's paradox within the limits of a genetic perspective of cancer causation. However, Peto's paradox is not a paradox, but a fact pointing to non-genetic and non-random etiologies for the neoplastic diseases that occur in all forms of life, including humans.