Why is breast cancer common but heart cancer rare?

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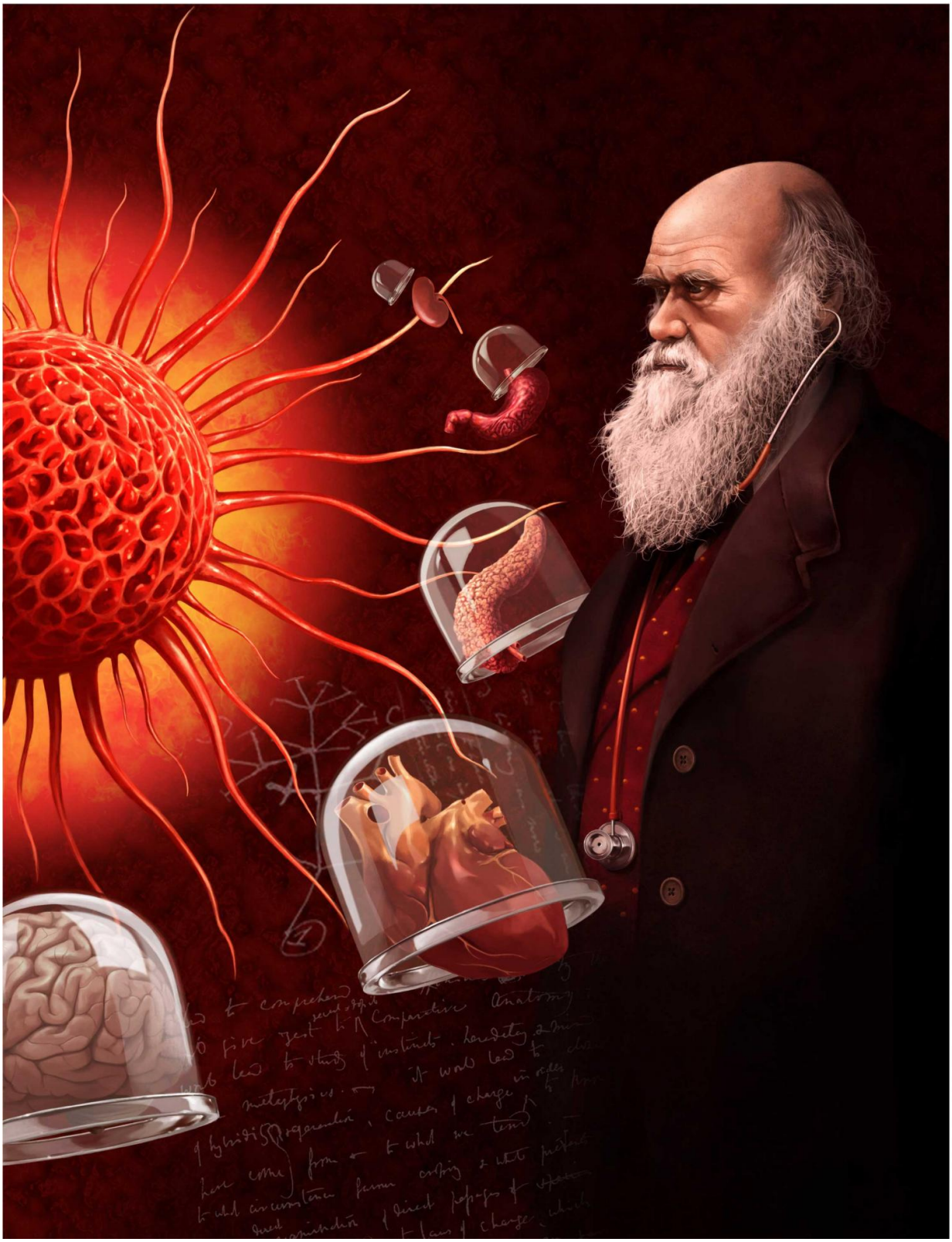

This artwork illustrates the idea that anti-cancer protections for organs are

influenced by natural selection and Darwinian fitness. Credit: Eric Pélatan

Malignant cancers strike certain organs, such as the colon or breast, more often than others. In an Opinion publishing August 9 in *Trends in Cancer*, researchers propose that this vulnerability in some organs may be due to natural selection. Humans can tolerate tumors in large or paired organs more easily than in small, critical organs, such as the heart, and so the larger organs may have evolved fewer mechanisms to defend against cancerous cells.

"The organs that are the most important to keeping you alive and capable of reproduction, such as the heart, brain, or uterus, may enjoy a better protection against cancer, all other things being equal," says Frédéric Thomas, an evolutionary biologist at the Center for Ecological and Evolutionary Cancer Research in France. "We are not saying that this is the main factor to explain the different susceptibility of organs to cancer, but it is a factor that contributes with others."

Many oncologists have explained the difference in rates of organ cancer by looking at either external risk factors, such as smoking or UV light exposure, or internal factors, such as how often cells must divide in an organ. Thomas and his coauthors, including senior author Beata Ujvari, an evolutionary ecologist at Deakin University in Australia, now propose this evolutionary theory to supplement the current understanding.

The team suggests that natural selection has favored strong anti-cancer protection for small organs that are critical to human survival and reproduction. "Organs that are large or in pairs could potentially accumulate larger numbers of oncogenic manifestations without being impaired, whereas small and important organs like the pancreas could be easily compromised with only a few tumors inside," says Thomas.

Therefore, so the theory goes, the pancreas should be better at defending against cancer compared to an organ like the kidney, if all other factors are equal. Anti-cancer protection mechanisms vary from organ to organ, but in general, they make an organ resistant to tumor formation.

The researchers also recommend that cancer biologists think of individual organs as specialized islands with their own environmental conditions (such as the level of oxygen, acidity, or water), where the survival of cancer cells depends on is the hospitality of the local environment. "Malignant cells are living entities—it's just impossible that they are not influenced by the ecological conditions," says Thomas. "It clearly means that certain organs are more favorable than others to malignant perturbation."

Thomas, Ujvari, and their colleagues are now working to test their hypothesis. "A complete analysis requires that we take into account all the possible confounding factors," emphasizes Thomas. "We cannot just look at existing statistics on cancer and the size of the organs and make a correlation to see if it works or not." Currently, the team is running a long-term experiment with mice to measure the accumulation of cancerous and precancerous mutations inside different organs. The research is part of a new international collaboration between Deakin University and the French National Center for Scientific Research (CNRS).

"It's a novel hypothesis that deserves to be explored," says Thomas. "We hope this paper will stimulate research in that direction."

More information: Thomas et al., "Evolutionary Ecology of Organs: a Missing Link in Cancer Development?" *Trends in Cancer*. www.cell.com/trends/cancer/ful … 2405-8033(16)30079-6. DOI: 10.1016/j.trecan.2016.06.009

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