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

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The authors want to find answer for why human has higher incident of cancer than other species. While multiple existing theories were discussed on the topic, the authors proposed a new hypothesis that the high inbreeding within the small human tribes by the dominant males of high social status could lead the narrowed genetic pool contributing to high cancer risk. The authors also argue that the high cancer incidence in post-reproduction females could benefit the communities by parental/grandparental care. Therefore, high cancer incidence in human is evolutionarily favored. The authors suggested to test their hypothesis by mining prehistoric human remains and using computational simulations.

Comments

1. As shown in authors description, higher cancer risk in humans than in many non-human species has been well observed. Different theories have been proposed to explain the reason. The authors' hypothesis is based pm low genetic diversity in tribes, and proposed to test the possibility by computational modeling. This approach has been well practiced in human genetic study. For example, human consanguinity, in some regions the rate reaches to up to 70%, has been practiced for thousands of years. If the decreased genetic pool contributes to the high cancer risk, these populations could be the nature model to test authors' hypothesis, through integration of the wildly available population-level cancer epidemical data. Analysis of actual human data would be much convincing than designing hypothetical model for computational simulations as the model could be artificial.
2. Massive genetic data from prehistoric human remains have been reported. The analysis of prehistoric human data can be valuable to test authors' hypothesis. However, most of the prehistoric human data were derived within the last 10,000 years. The definition of "prehistoric human" needs to be well determined in order to test the hypothesis with the prehistoric humans within their defined timing range. Otherwise, it will not provide much useful value. Further, it will be very difficult to find the cancer evidence in prehistoric human remains. Therefore, it might be better to analyze the deleterious variants in cancer predisposition genes, which are known to cause high cancer risk, such as the deleterious variants in BRCA1 that lead to 80% of cancer risk during carriers' lifetime. Such data can be much easier to be identified than cancer evidence. And the focus on traditional oncogene and tumor suppressor can provide limited information. Instead, identification of deleterious variants in hundreds of genes in different DNA damage repair pathways can reflect better the link between human mutation and human cancer risk.