

Review of: "Somatic evolution of Cancer: A new synthesis"

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Potential competing interests: No potential competing interests to declare.

The article by Ulfat Baig et al. titled "Somatic evolution of Cancer: A new synthesis" is interesting and faces significant debate on cancer onset and biology, introducing new views.

However, I would raise some significant concerns regarding the rational framework of this manuscript: it would be of great interest if a large number of ideas were better organized to shape the new vision of the origin of cancer proposed by the authors. I ask for greater clarity in the exposition of the logical sequence, starting from the introduction, to better understand the work's content and objectives. Moreover, given the ambitious goals posed by the authors, i.e., to revise the theories of carcinogenesis to pave the path for a new vision, a deeper analysis of the literature for each theory is recommended. Thus, the authors should draft the manuscript by discussing a few insights that are deepened in theory and discussed in detail to bring out the innovative component of the reasoning.

Major concerns:

- 1) The introduction has to be more aligned with the article's rational framework to anticipate the reader to the critical points of the discussion sustained throughout the manuscript;
- 2) The authors must discuss different theories following a deeper description of each biological process in physiological or pathological conditions. For instance, critical sentences such as "remarkable similarity in cancer and wound healing pathways" must be adequately discussed following a bottomless description of the molecular mechanisms starting and ending the wound healing process by identifying whether these can trigger a "wound that never heals." Similarly, the analysis of the oncologic mechanisms driven by the tissue microenvironment on the cell must be mentioned in physiology or transformation (see Weaver VM articles doi: 10.1016/j.devcel.2021.05.011).
- 3) The text requires a significant language revision to be more readable