Review of: "Introduction to Evolutionary Cancer Cell Biology (ECCB) and Ancestral Cancer Genomics"

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Potential competing interests: No potential competing interests to declare.

The article introduces the concept of Evolutionary Cancer Cell Biology (ECCB) and discusses its perspective on the origins of cancer, challenging conventional notions in cancer research. The author aims to clarify and contrast ECCB with a recently reviewed article titled "Somatic Evolution of Cancer: A New Synthesis." The article is comprehensive, delving into the evolutionary aspects of cancer genomics, the role of polyploidy, and the implications for cancer therapy.

Strengths:

- **In-depth Exploration:** The article provides a thorough exploration of ECCB, tracing its roots back to evolutionary theories proposed by Davies and Lineweaver in 2011. It builds on the concept, incorporating findings from various researchers over the past two decades.
- **Cohesive Framework:** The author successfully presents ECCB as a cohesive framework, connecting ancient cellular mechanisms to cancer development. The incorporation of phylostratigraphic studies, comparative genomics, and deep homology contributes to a unified understanding.
- **Critical Evaluation of Existing Hypotheses:** The article critically evaluates the "New Synthesis" hypothesis, pointing out its limitations and proposing the ECCB perspective as a more comprehensive alternative.
- **Integration of Evolutionary Concepts:** The incorporation of concepts such as asexual speciation, deep homology, and the comparison with the parasitic Entamoeba cell system enriches the evolutionary perspective on cancer.

Areas for Improvement:

- **Clarity of Presentation:** While the article is rich in content, the complexity of the subject matter may pose a challenge for readers unfamiliar with ECCB. Improved clarity in presenting key concepts and their interconnections could enhance accessibility.
- **Evidence and Citations:** Some statements, especially those related to specific evolutionary timeframes and the relationship between cancer and ancient cell systems, could benefit from more direct references or citations to specific studies. This strengthens the credibility of the claims made.
- **Relevance of Terminology:** The use of terms like "ancient aGRN" and "protist hyperoxia" might be daunting for readers without a deep background in evolutionary biology. Consider providing clear definitions or simplifying complex terms for broader comprehension.
- **Balanced Discussion:** While the article provides a compelling argument for the ECCB perspective, a more balanced

discussion acknowledging potential counterarguments or areas of uncertainty would strengthen its scientific rigor.

Conclusion:

The article presents a thought-provoking exploration of cancer from an evolutionary standpoint, introducing ECCB as a novel and comprehensive framework. Strengthening clarity, providing more explicit evidence for certain claims, simplifying complex terminology, and incorporating a more balanced discussion would enhance the overall impact and accessibility of this intriguing perspective on cancer biology.