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.

Vladimir F. Niculescu indeed presented a fascinating article, and investigated the multifaceted and mysterious dominion of cancer biology, accentuating the precincts of conventional hypotheses on cancer by introducing Evolutionary Cancer Cell Biology (ECCB) as a novel branch of oncology. The evolution of a gene is not limited to a specific species but occurs through different groups/domains, as all complex life forms (unicellular/multicellular) including humans evolve as a result of evolution from the simplest and most primitive groups that originated on earth. To correlate this theory in terms of all known cancer hallmarks, we need more experimental data.

Here are the core points that provide strength to the article:

- The basic framework supported by paleontological and cancer genetics studies explaining evolutionary events
- Establishing cancer as an evolutionary process involving adaptations over time and surroundings rather than merely assuming it is a genetic mutation.
- ECCB highlights homologies (similarities) between processes like carcinogenesis, tumorigenesis, metastasis, gametogenesis, and early embryogenesis.

Although the article is well framed but incorporation of the following suggestions will enhance the impact of this fascinating viewpoint on cancer biology:

- Components of gene regulatory networks (GRN) must be explained to have insights into their role in the emergence of proliferative cell phenotypes.
- ECCB must be supported with more empirical evidence, and experimental data, providing a more concrete foundation.
- Long-term evolutionary dynamics highlighted by ECCB, might not always align with imperative and immediate clinical applications.
- Lack of potential to support direct patient outcomes and practical interventions.
- less established framework in bridging gaps between evolutionary theory and medical applications
- The present article is stuffed with enormous information on ECCB in a concise /brief manner; it must be elaborated for better understanding.
- A brief description of shared molecular pathways and gene networks, between cancer progression and normal developmental processes can be added.

A brief description of the ECCB concerning the evolution of life can be explained with a figure, to provide a better

understanding of the concept to readers, who are unfamiliar with the correlation of evolutionary biology with cancer biology. Overall the article is a good attempt to view cancer from a new perspective, that combines evolutionary history, genetics, cell biology, and molecular biology to redefine the entire framework of the oncology field.