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Peer Review

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

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This preprint **"Introduction to Evolutionary Cancer Cell Biology (ECCB) and Ancestral Cancer Genomics"** is an ambitious, concept-heavy synthesis that argues for an evolutionary framework of oncogenesis (deep ancestry of "cancer programs," emphasis on stem-cell–like origins, polyploidy/PGCC biology, and a reduced centrality of somatic mutations), and it usefully compiles multiple evolutionary-cancer threads into a single narrative; however, its main weaknesses are that many key claims are **presented as conclusions without direct, testable evidence** (e.g., "non-mutational" primacy, DSCD cell-of-origin generalization, and broad homology claims), the paper **blurs review vs. advocacy** (it partly reads like a rebuttal/opinion piece to another Qeios article rather than a neutral research article), and it **lacks operational definitions and falsifiable predictions** (what observations would refute ECCB, what biomarkers/assays define DSCD cells, what datasets demonstrate causality vs. correlation in gene-age upregulation). To strengthen it, the author should: (1) clearly separate *hypothesis framework* from *evidence*, (2) propose **specific, falsifiable predictions** (e.g., prospective single-cell multi-omics signatures, lineage tracing criteria, PGCC functional assays, mutation-burden stratified tests), (3) include a **systematic review-style methods section** for literature selection and weighting, and (4) present **direct comparative data** (or re-analyses of public datasets) linking proposed ancestral gene modules to reproducible tumor phenotypes and clinical endpoints, with clear alternative explanations addressed.

Declarations

Potential competing interests: No potential competing interests to declare.

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