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Peer Review

Review of: "Mechanisms of Selection on Cancer-Causing Mutations"

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The review article **"Mechanisms of Selection on Cancer-Causing Mutations"** presents an interesting evolutionary perspective that shifts focus from mutation accumulation to context-dependent selection, and its strength lies in proposing mechanistic hypotheses linking tissue microenvironment, stem cell dynamics, and lifestyle factors to cancer evolution. However, the article shows several weaknesses, particularly its strong reliance on theoretical speculation and a hypothesis-driven narrative rather than a systematic or critical synthesis of experimental and clinical evidence, which reduces scientific robustness. The review lacks a structured methodology for literature selection, risk of bias assessment, and quantitative integration of supporting data. Some mechanistic links (e.g., lifestyle monotonicity and growth factor deficiency) are extrapolated without sufficient causal validation, and many proposed experimental directions remain conceptual rather than technically detailed. Additionally, the manuscript would benefit from clearer differentiation between established evidence and speculative hypotheses, inclusion of graphical mechanistic models, and stronger integration of translational implications such as therapeutic targeting or biomarker development. To improve the article, the authors should adopt a systematic or semi-systematic review framework, incorporate meta-analytic or comparative experimental data, provide clearer mechanistic validation pathways, and strengthen the discussion of clinical relevance.

Declarations

Potential competing interests: No potential competing interests to declare.

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