

Peer Review

Review of: "The tumour microenvironment in BRCA1/BRCA2 hereditary breast cancer and the role of epigenetics in its regulation"

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The manuscript provides a timely overview of how BRCA1/2 pathogenic variants may shape the tumour microenvironment and discusses the potential involvement of epigenetic regulators, particularly LSD1. The topic is indeed relevant, and the authors have surveyed a broad body of literature. That said, several aspects could be strengthened to improve the coherence and scientific weight of the review.

Major Comments

1. Much of the text summarises individual studies in isolation. It would help readers if the authors could synthesise the evidence—highlighting areas of consensus, points of conflict, and gaps—especially when comparing hereditary versus sporadic breast cancer. The current version reads more like a catalogue of studies than an integrated narrative.
2. Some statements imply a direct causal role for LSD1 in the regulation of BRCA2. While the link between LSD1 and BRCA1 repression is well supported, evidence for BRCA2 involvement appears limited and somewhat speculative. These claims should be moderated or clearly framed as hypothetical.
3. The two major sections (TME changes vs. epigenetic mechanisms) are described clearly, but the manuscript would benefit from a more explicit explanation of how epigenetic regulators (including LSD1) help maintain specific TME phenotypes in BRCA-mutated cancers.
4. Given the density of information, schematic diagrams summarising key pathways—e.g., BRCA1/2-related TME changes or the roles of LSD1—would greatly improve clarity.
5. Several cited studies are relatively old. Incorporating more recent work, particularly those published

between 2022 and 2024 on cGAS/STING signalling, microRNA regulation, and LSD1-targeted therapies, would strengthen the review.

Minor Comments

6. Repeated discussions of EMT, hypoxia, and inflammatory signalling appear in multiple sections; these could be consolidated for conciseness.

7. Some long paragraphs may be easier to follow if shortened or split.

8. Please ensure consistent formatting and define all abbreviations at first mention.

Overall, the review covers an important area, but clearer integration of the evidence and a more balanced interpretation—especially regarding LSD1—would improve its suitability for publication.

Declarations

Potential competing interests: No potential competing interests to declare.