Peer Review File

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Reviewer A

Comment 1: One is novelty. Fontemaggi et al (2021) recently published a review on circRNA that included breast cancer. The authors should demonstrate how this dive is separate from what Fontemaggi et al did.

Reply: The review published by Fontemaggi et al in 2021 aims to report the results of novel circRNA functions and molecular regulation, beyond ceRNA. Their article highlights the new functional mechanisms of circRNAs, such as 1. A Variety of circRNA/RBP Complexes with diverse functions 2.Translation of circRNAs 3. Regulation of Immune Functions by circRNA 4. Functions of circRNAs in the Exosomes 5.circRNAs in the Drug Resistance. In the process, they mention several circRNAs that play a role in breast cancer, but this is incomplete for circRNAs in breast cancer.

In contrast, we innovatively start from circRNA function, based on the diagnosis and treatment of breast cancer, and provide a more comprehensive and in-depth overview of the most recent and relevant results on the intrinsic molecular mechanisms of circRNA in breast cancer. We summarize four major mechanisms of circRNA action in breast cancer, including circRNA as miRNA sponges, circRNA as translation template, circRNA binds RBPs, and circRNA regulates gene expression. At the same time, we illustrate 20 studies, including CircRRM2 and CircBRWD3, etc., and provide our summary and outlook. The scope, content, and research directions reviewed in our article are different from those of previous articles, and it is clear that this is a novel and research-worthy article.

Comment 2:There are several spelling and grammar mistakes, and the overall language makes it hard to follow. I strongly recommend the authors utilize a copyeditor to go through and fix all the mistakes and improve the flow.

Reply: We are sorry for these mistakes in the article. We carefully reworked the article using a copyeditor to correct spelling and grammatical errors and improve the flow of the article.

Changes in the text: We have modified our text as advised. （See red changes in the article）

Comment 3: Table 1 needs more context and is impossible to read in this state

Reply: Thank you for this comment. We've taken your suggestion and added context to the article

Changes in the text: We have modified our text as advised. （See Line 64-69.）

Comment 4: There should be a space after every ".". Common error throughout the text.

Reply: We have corrected all grammatical errors and missing spaces in the article using the document editor. Again, we sincerely apologize for these errors.

Changes in the text: We have modified our text as advised. （See red changes in the article）

Comment 5：Numbers are needed when making comparisons.

Examples; line 158 "...expression was upregulated." By how much? 2-fold? 10-fold?

Line; 47 "...have a longer half-life than linear RNAs." By how much? What is the half-life of each? Several examples of these.

Reply: We really appreciate this suggestion. As you say, we do need some numbers to make the article more convincing when making comparisons. We reviewed the literature again and added some numerical comparisons, but in some comparisons, we were unable to change our article due to the lack of relevant data in the original literature. Thank you very much for this comment!

Changes in the text: We have modified our text as advised. （See line 48-49, line188-190, line 231-232 ）

Comment 6:Conclusion and future prospects does not really do a good job summarizing the article or bring the article into the context of the field. It should focus on the bigger picture and how the information on circRNA presented here really informs the reader on its importance. The reader should read this part and feel like they have learned something important and new.

Reply: We took your suggestion and made a new conclusion and future prospects. We hope that you will check it again, and if it is still not appropriate, you are welcome to criticize and correct it again.

Changes in the text: We have modified our text as advised. （See line 430-452）

Reviewer B

1. Please expand the Abstract to at least 200 words.

Reply: We've expanded the abstract section.

Changes in the text: We have modified our text as advised. （See line 20-44）

2. Based on the journal guideline, the “Conclusion and Future Prospects” section should be modified to “Conclusions” section.

Changes in the text: We have modified our text as advised. （See line 444）

3. “Previous studies have demonstrated that SMARCA5 plays a critical role in regulating DNA
repair processes and maintaining genome stability, and affects breast cancer progression[54],…”“Previous studies have demonstrated the crucial role of circRNAs in regulating the proliferation,invasion, metastasis, and drug resistance of breast cancer cells[6].”
Studies were mentioned, but there is only one reference cited. Please confirm whether more references are needed.

Reply: These two places do need more citations, which we have rechecked and added.

Changes in the text: We have modified our text as advised. （See line 64, line 431）

4. circRNAs should be defined upon first use in the Main Text.

Changes in the text: We have modified our text as advised. （See line 57-58）

5. in vitro/in vivo/genes should be italicized in the text.

Changes in the text: We have modified our text as advised. （See line 136, 154, 157, 163, 169. 207, 244, 249, 274, 328, 337, 348, 408, 421, 442 ）