Reviewer’s report

Title: Metformin enhances tamoxifen-mediated tumor growth inhibition in ER-positive breast carcinoma

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Reviewer: Hao Zhang

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Major Compulsory Revisions

The present study wants to demonstrate the synergistic effects of metformin on breast cancer cells by cell survival, DNA replication activity, plate colony formation, soft-agar, flow cytometry and nude mice model assays. And the authors demonstrated the effects induced by tamoxifen were enhanced by metformin. The authors further showed that the bax/bcl-2 apoptotic pathway and the AMPK/mTOR/p70S6 growth pathway were involved in this progress. The data are interesting and solid. However, the authors have to improve the current manuscript:

1. The authors have not improved the quality of this manuscript according to the suggestions by the last reviewer very well.
2. It’s not enough to draw the conclusion: “metformin and tamoxifen have synergistic effects”, since it could be additive effect rather than synergistic effect. The combined effect should be examined by appropriate methods.
3. It seems that the authors have not over corrected this manuscript seriously. In the present manuscript, there are several low-level errors:
   1) Page4, line 2, did diabetic patients not receiving this drug?
   Page4, line 3, This sentence “most of these women were receiving endocrine therapy” does not seem to connect with the context.
   2) Page10, line5, phosphorylation of AMPK was significantly decreased?
   Page10, line5, where’s the data of MAPK and AKT?
   3) Page11, the data of tumor growth is in figure 6C not figure 6B !!!
   And the data of tumor weigh is in figure 6B not figure 6C !!!
   4) There is a spelling mistake in figure 1A, “tamixifen” should be “tamoxifen”.

4. In the abstract, “a large number of patients are low reactive or resistant to tamoxifen”, these patients are ER positive? It’s better to cite the references.
5. The authors should explain why they selected 5mM metformin and 5 µM or 10µM tamoxifen for further research.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests