Reviewer's report

Title: Targeting cellular metabolism by 3-Bromopyruvate improves Tamoxifen Cytotoxicity in Breast Cancer Cell Lines

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Reviewer: Michael Chan

Reviewer's report:

The manuscript by Attia et al examined the effect of Tamoxifen, an anti-estrogen on the cytotoxicity of 3-Bromopyruvate, a glycolytic inhibitor, to breast cancer cell lines (MCF7 and T47D). The authors performed several cell line examines to examine the combination effect of Tam and 3-BP on survival, expression of oxidative stress marker, caspase, VEGF, MMP as well as in a xenograft mouse model. Although the results are potentially interesting, the manuscript is well-organized and further experiments are required to confirm the result.

Major Compulsory Revisions:

1. The authors should explain clearly the rationale of conducting each experiments. For example, before describing the effects of TAM/3-BP on oxidative stress markers (MDA, rGSH), they should explain briefly why they conduct this experiments.

2. On page 10, the authors examined the expression of VEGA-A with title "the effect of 3-BP, TAM on their combination on angiogenesis". However, it might be over-stated as they only examined the expression of VEGF but not angiogenesis. To examine angiogenesis, the authors should perform either co-culture experiment using HUVEC cells or culturing HUVEC cells using the conditioned media from the treated breast cancer cell lines;

3. The western blot of Figure 4E, F is sub-optimal. To examine apoptosis, the authors should perform flow cytometer using annexin V/PI assay or PI-sub G1 peak assay;

4. Figure 10 cannot be found;

Minor essential revision:

1. The format of references are not consistent.

2. There are several typos and grammatical mistakes

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited
**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.