Reviewer's report

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

Version: 2 Date: 21 July 2015

Reviewer: Deliang Guo

Reviewer's report:

In this manuscript, Yasmin Attia et al. investigated the combination therapeutic effects on breast cancer cell lines by using glycolysis inhibitor 3-bromopyruvate and tamoxifen. The authors showed that 3-bromopyruvate treatment enhanced the toxicity effects of tamoxifen in MCF7 and T47D cell lines. They measured cell proliferation, apoptosis effectors and in vivo xenograft tumor growth by drug alone and combination, and made conclusion that 3-bromopyruvate could enhance tamoxifen therapeutic effects in breast cancer cell lines. It is interesting story by using glycolysis inhibitor with endocrine therapy drug. However, there are major issues for the manuscript and authors need to pay attention to improve it as discussed below.

Major comments:

1. In Results section, the writing needs to be greatly changed and improved. Each result section needs to have a title that delivers a major conclusion, not describe what to do like a legend title. In addition, should write results smoothly and briefly bring the rational. Results section needs to do a major revision.

2. Figure 2. The doses for both drugs used were pretty high, but the combination effects were not very strong.

3. Figure 4. For panel A-D, should show western blot data. For Panel E, it looks Caspase -7 decreased in the combination treatment. For Panel F, the increase of Caspase-7 was not significant.

4. Figure 6, All western blot data were not clear. Although there were quantification analyses, the western blot bands were not really changed between control and drug treatment.

5. Figure 7, Panel F, western blot data were not clearly changed. For Panel G and H, 3-BP treatment increased MMP-9 levels, but quantification showed decrease.

6. Figure 8. Should show tumor growth curve, or at least final tumor picture. And stain CD31 to show vasculature effects of drug treatment. In addition, why choose Ehrlish 346 carcinoma, instead of MCF7 and T47D cell lines, for xenograft study? In vitro and in vivo cell lines were not consistent.

Minor points:

1. In the manuscript, please try to keep consistency when the hour is short for “h” or “hrs”, still “20µM” or “20 µM”.

2. There are two G panels in the figure 7. Please remove one.
3. For title, please consider changing to ‘Targeting glycolysis by 3-bromopyruvate…’ to better deliver the drug effect.

**Level of interest:** An article of limited interest

**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:**

No competing interests to this paper.