Reviewer’s report

Title: Fenofibrate induces apoptosis of triple-negative breast cancer cells via activation of NF-κB pathway

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Reviewer: Tiffany M Phillips

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Overall the authors present a well designed experiment and clear data to support their hypothesis. The data demonstrate that fenofibrate is able to induce apoptosis both in vitro and in vivo in TNBC and show a relationship of this to NFκB signaling. The consistency between in vitro and in vivo data strengthens the manuscript.

Major Compulsory Revisions

1. The authors use GW6471 to inhibit PPAR-alpha in Figure 3A and 3B to show there is no dependence. However, there is no data/figure to verify the inhibition of PPAR-alpha or to what level it is inhibited.

2. The authors explore NFkB signaling in Figure 3, however there is no discussion about TFIIB, what it is, why it is used and its role. Also there are no nuclear loading controls.

Minor Essential Revisions

1. It is difficult to distinguish the lines in Figure1A. Color may help clarify this figure.

2. The sensitivity of the cell lines to fenofibrate does not clearly distinguish two populations. Why might a TNBC line like MDA-MB-436 behave similarly to HCC1937? Figure 1B does not show any significant difference so how might this be explained.

3. Discussion and data to show the p53 and PTEN mutational status of these TNBC cell lines should be addressed. There are studies showing that p53 mutational status may subdivide TNBC cells into two distinct populations. Further, PTEN status has also been linked to response of TNBC to therapy. Since the authors examine cell cycle, apoptosis and Akt signaling, it only makes sense to address these additional potential mutations and discuss how they may play a role in this response of TNBC.

4. The manuscript contains some grammar and spelling issues that should be addressed prior to publication.

Discretionary Revisions

1. The data would be strengthen by performing the set of experiments in more
than just the one cell line (MDA-MB-231). How do these experiments compare to one of the less sensitive TNBC cell lines like MDA-MB-436? Do you still see the same signaling mechanisms in these less sensitive lines? Is this signaling seen in any of the non-TNBC lines?

2. Discussion about the timing of the cell cycle arrest would improve the reasoning. The western blots show distinct differences in the 6 and 12 hour time points in Figure2D and the cell cycle is analyzed at 24 and 48 hours in Figure2C. Discussing why these time points were chosen would help.

**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 have no competing interests.