Reviewer's report

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

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Reviewer: Chann Lagadec

Reviewer's report:

I reviewed the manuscript from Li et al. untitled: Fenofibrate induces apoptosis of triple-negative breast cancer cells via activation of NF-kB pathway”.

Authors used several breast cancer cell lines with various phenotype to show that fenofibrate could reduce growth of breast cancer cells. They found that MDA-MB-231 shows an higher sensitivity to fenofibrate and use it as a model for following experiments. They show apoptosis and cell cycle analysis, in parallel with western blot of proteins involved in each process. Then, they identify NF-kB as involved pathway on finofibrate-induce apoptosis, and not PPARa the main target of fenofibrate. Interestingly, authors analyze the effect of the treatment on MDA-MB-231 by globale RNA expression analysis. They finally analyze the effect of fenofibrate of tumor growth in nude mice, checking for tumor growth and several vital components.

Major comments:

Manuscript and results are poorly presented. as example of Figure 1.A. with is unreadable...

Several experiment do not show repeat (Figure 2A and C), or so small SD that they might be technical repeats and not biological repeats?

The authors used MDA-MD-231 as “representative” for the effect of fenofibrate on breast cancer cell lines while it the most sensitive to this drug? ?? It might be used as a model to study the effect of fenofibrate because of it high in vitro response to treatments... however in vivo treatment show really few effect of fenofibrate on tumor growth or apoptosis induction. Interesting question would also be, what is the difference between TNBC and other subtypes which allow this difference on treatment response?

Western blot are really nice and well performed, however details are required in M&M to be reproduced by other, as lysis buffer formulation

Authors performed western blot on nuclear and cytoplasm fraction... method has not been provided.

Array analysis, unfortunately, do not add any usable information other than cells are stressed and might die (things that they are not really doing BTW)...

In vivo data are not really convincing, especially regarding the starting day of the treatment (7 days after cells injection) and the frequency of the treatment (every
Tumor mass represent up to 15% of mice body weight, however, the significant difference of tumor mass between control and treated group (1g = 5% of mice body) is not reported to global mice weight... not explanation has been provided?

Even if apoptosis induction in vitro is significant (23% at 72h), the in vivo induction is really low... not explanation has been provided.

Figure legend are badly detail or not detail at all... as an example, figure 6, the abbreviations WBC, HGB, PLT, ALT, AST and BUN are not defined (neither they are in the text).

Weak effect in mice experiment might hind effet on survival... Kaplan-Meier graph might be informative

Figure 5 legend: “suppressed”... tumor growth is not suppressed at all... slow down!

Minor comments:

In introduction, authors mentioned chemotherapy as the unique choice for TNBC patients... what about surgery and radiotherapy?

M&M- cell culture: SK-BR3, MCF-7, ... and MDA-MB-468 “were” (and not was)

Cell lines status has to be provided

Cell-cycle analysis: need details on concentration for RNAse A and PI

Western-blot: what is the blocking buffer or other buffer used? what is the lysis buffer?

Nude mice: 200 mg/kg were (and not was)

Figure 1C... might need a lower magnification

p11: “could inhibit cell proliferation, finally resulting in death”... there is no sequential experiment allowing that conclusion

Effect on Cdk4: no effect can be observed

Figure 2: no legend for dot blot... no legend for histograms

Figure 2: Why did authors use 7-AAD staining if not used for further analysis?

Figure 4B, switch diagram to visually show a decrease

Figure 5 E, need magnification for control

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:
I declare that I have no competing interests