Reviewer’s report

Title: Mitochondrially targeted vitamin E succinate efficiently kills breast tumour-initiating cells in a complex II-dependent manner

Version: 2

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Reviewer: Jaroslav Truksa

Reviewer’s report:

I have read the article entitled “Mitochondrially targeted vitamin E succinate efficiently kills breast tumour-initiating cells in a complex II-dependent manner” with great interest. The data are sound and I recommend minor revisions. Yet, I have a few comments that the authors should take into account.

1. The authors use the MTT method to assess the effect of MitoVES on cellular proliferation. Since this method relies, at least partially, on the oxidative capacity of mitochondria, isn’t it counterintuitive to use such method for assessing the effect of compounds that affect the mitochondrial oxidative respiration?

2. Figure 2G shows PARP cleavage and activation of caspase 3 in cells treated with MitoVES. Yet, it is clear that control samples from sphere samples do show signs of cleaved C8 and C9 similarly to MitoVES treated samples. Is there any explanation for this? Has this been reproduced in the MCF7 cells as well?

3. Labelling of the panels in Figure legends is inconsistent, in some figures the panels are shown as (x) at the end of the sentence while in others they are without brackets at the beginning of the sentence, this should be unified.

4. The changes in the mitochondrial (super)-complexes are very weak and I would think that the only significant difference is seen in the complex IV (super)complexes, so I suppose these changes are probably not causing the apoptosis but are rather an accompanying process.

5. There are references to supplementary data which were not present in the actual manuscript. Is that any technical issue?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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