Reviewer's report

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

Version: 2

Date: 25 February 2015

Reviewer: Manish Chourasia

Reviewer's report:

Neuzil et al have attempted to kill breast tumor initiating cells, using mitochondrially targeted vitamin E succinate. The manuscript is extremely well drafted and the figural representation of data is pleasing. I feel the authors need to address a generalized query and few technical glitches.

Comment No. 1: Mitochondrially targeted vitamin E succinate seems to be a focal area for the authors as they have a previously published manuscript in JBC elucidating its mechanism of action in Human T lymphoma Jurkat cells. It is also praise worthy that the authors have mimicked the implications of their findings in breast cancer cells. However, I feel it is highly imperative to draw an articulate conclusion regarding the prospects of the compound. Does it stand a chance to emerge as a frontline cytotoxic compound, or, will it be better off as a smart carrier moiety which synergizes the cytotoxic thrust of well established compounds. The explanation should be included in the final version of the draft, as it can serve as a guiding light to researchers engaged in tackling cancer. Additionally, is there any rationalization as to why MitoVES was efficient in sphere cells and not adherent cells?

Comment No. 2: Table1, which depicts the IC50 values, does not give any units (nM or µM). The textual portion of cytotoxic assay states usage of Doxorubicin, however Doxycycline (an antibiotic) is shown in the table. What is meant by n.d.in table? Doxorubicin and paclitaxel are amongst the most potent cytotoxics against MCF 7 cells (several reports are available, quantifying their activity). It would be of greater comparative significance, if their IC50 values were also presented.

Comment No. 3: Line 92- primer sequence and PCR specificities were not mentioned.

Comment No. 4: Line 113- MTT crystals ‘were’ dissolved in DMSO. Correct the statement as MTT is a water soluble dye, and it is its reduced form formazan which is dissolved in DMSO.

Comment No. 4: Minor Typographic errors like:
Line 224- Fig A “&” B
Line 466- brackets not given (E), (F), (G)
Line 480 “(C)”
Line 484- (F), line 485- ‘(G)’
Line 522- : “derivefd from results whon in panel A..” spelling error.
Comments No. 5: In fig 2(G) Caspase 9 (C9) control group also causes equivalent inhibition of adherent cells. Why would that be? In fig 2(G) the graph below caspase 9 should be caspase 3 graph rather than caspase 8.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests