Reviewer's report

Title: Phenethyl isothiocyanate upregulates death receptors 4 and 5, sensitizes TRAIL-induced apoptosis, and inhibits proliferation in human cancer stem-like cells

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Reviewer: Huey-Jen Lin

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Dr. Dey and authors have demonstrated a potent dietary anti-cancer drug namely Phenyl Isothiocyanate (PEITC) that could combat cervical cancer stem-like cells via induction of apoptosis. Though this report was well written with logical experiment design and accompanied with solid data for supporting conclusions, the following concern shall be brought to authors’ attention for improving the quality of the article.

Major Compulsory Revisions

1) The whole study was built upon the findings from one cervical cancer cell line known as HeLa which might be somewhat insufficient. As the following cervical cancer cell lines are commercially available from ATCC, it might be feasible for authors to include another cell line to provide an un-biased study.
   a. Ca-Ski, ATCC CRL-1550
   b. DoTc2,-4510 ATCC CRL-7920
   c. SiHa, ATCC HTB-35
   d. C-33-A, ATCC HTB-31

2) A lack of normal control is another concern. Hence, commercially available non-malignant cervical epithelial cells (from normal individuals) are recommended to be involved with this study, for revealing the background cytotoxicity effect from PEITC and from TRAIL on normal cervical cells.

3) Biomarkers for identifying cancer stem-like cell remains rather inconclusive and each marker might enrich a distinct subset of cancer stem-like cell population.

   A recent publication reported in Oncotarget. 2013 Dec;4(12):2462-75 entitled: “High aldehyde dehydrogenase activity identifies cancer stem cells in human cervical cancer” demonstrated that a subpopulation of cervical cancer cells retain high aldehyde dehydrogenase (ALDH) activity that characterizes a subpopulation of cells with cancer stem-like cell (CSC) properties. Therefore, authors are encouraged to substantiate their findings in the ALDH-enriched CSC subpopulation.

Minor Essential Revisions
Data presented in the paper could be somewhat overly interpreted. For example, as shown in Figure 4B, elevated expression of DR5 was rather insignificant, after a combined treatment with PEITC and TRAIL. Authors might weaken their tone and further provide alternative explanations.

**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.