Reviewer’s report

Title: Resveratrol protects leukemic cells against cytotoxicity induced by proteasome inhibitors via induction of FOXO1 and p27Kip1

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Reviewer: Alessandra Mocali

Reviewer’s report:

This manuscript by Xiao-Fang Niu et al. describes the protective effect of resveratrol against cytotoxicity induced by proteasome inhibitors in leukemic cell lines. Literature on various effects of resveratrol as anti-cancer compound is very rich, and this paper is of a sufficient interest in the field. Data presented are consequential and sufficiently well presented, however I think that several revisions are needed prior to be accepted for publication.

There are two Major Compulsory Revisions:

1) In the first paragraph of Results authors say that “resveratrol alone caused no obvious apoptosis on K562 cells within 24h when applied even at concentrations of 100 µM (Figure 1D), indicating that although it was sufficient to inhibit proliferation, resveratrol per se was not sufficient to induce apoptosis in K562 cells within 24h.” Other authors (Chakraborty et al., Cancer Sci, June 2008, vol. 99, no. 6, 1109–1116) reported that resveratrol induces apoptosis in K562 cells. They used 40 µM resv for 24, 48 and 72h. I think that it would be better to repeat experiments at least after 48h, otherwise authors should explain why they performed experiments only for 24h. This citation would be also added.

2) Data show that resveratrol acts as antagonist against MG132 through the blockage of cell cycle progression at the G1/S transition and thus preventing the cell from proliferation. However, this anti-proliferative effect might be positive for cancer cell treatment with proteasome inhibitors, should it correlate with cell commitment to differentiation. This hypothesis would request some discussion and/or experimental evidence by the authors (e.g. the expression of differentiation markers). Lacking in vivo experimental evidences and also for above reported reasons, expressions as “attenuation of antitumoral action” by resveratrol should be replaced with “attenuation of apoptotic effect of proteasome inhibitors”.

Minor Essential Revisions:

1) Some more recent citations on the usage of proteasome inhibitors in cancer therapy would be added and discussed

2) There are some citations without the year of publication.

3) All the text requires some editing, in particular:

Abstract:
- Line 2, “the anticancer actions of several other cancer drugs” should be: ....some conventional chemotherapy drugs
- Conclusions section of the Abstract is too emphasized, while not sufficiently supported by experimental data.
Methods: Last sentence “all experiments were repeated three times, and data were expressed as the mean ± SD from a representative experiment” contains a mistake.

**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 declare that I have no competing interests