Reviewer’s report

Title: Phosphatidylinositol 3-kinase inhibitor induces chemosensitivity to a novel derivative of doxorubicin, AD198 chemotherapy in human bladder cancer cells in vitro

Version: 0 Date: 20 Aug 2015

Reviewer: Ghanshyam Upadhyay

Reviewer’s report:

The work by Dmitriy et al., is an attempt to to compare the efficacy of Dox and AD198 on human bladder cancer and explore their mechanisms in inhibition of the human bladder cancer cells in vitro. They used 2 human transitional cell carcinoma (TCC) cell lines, T24 and UMUC-3, to make their point. Although the results exhibit the similar mechanism of action for both the drugs, the efficacy of in modulating the various cellular events like cell survival, ROS generation, apoptosis and MAPK pathways are variable. The results showed that AD198 is superior to Dox in promoting cell survival and ROS generation where as Dox is better in inducing apoptosis and phosphorylation of AKT1. I also noticed a variable behaviour of the drugs in two cell lines. In my view, although the findings reveal that AD198 could be effective in the treatment of bladder cancer, the study can't be considered conclusive without in vivo studies. Additionally, the inclusion of animal data will illustrate the clear picture and will rule out the confusion due to variable results in cell lines.

Additionally, I will suggest to authors to delete the following sentence or include the appropriate data/reference for it.

"AD198 might act through different apoptotic mechanisms"

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Unable to assess

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I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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