Reviewer’s report

Title: Smac Mimetic-Derived Augmentation of Chemotherapeutic Response in Experimental Pancreatic Cancer

Version: 1 Date: 11 June 2010

Reviewer: Haoxing Xu

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Awasthi et al investigated whether Smac mimetic (JP1201), a presumed pro-apoptotic agent, could sensitize the anti-tumor effects of standard chemotherapy agents, such as gemcitabine (Gem), doxorubicin (Dox), and docetaxel (DT). To test their hypothesis, the authors performed experiments both in vitro (cancer cell lines) and in vivo (animal tumor models). Using a cell viability assay and an apoptosis assay, they found that JP 1201 exhibited obvious anti-proliferation and pro-apoptotic effects. Animal studies suggested that Smac mimetic could significantly enhance chemotherapy responses and improve the survival of mice with pancreatic cancer. The results are very interesting and potentially important for the clinical treatment of pancreatic cancer. The paper is very well written and data are clearly presented. The content of the manuscript is very relevant for the journal. I only have few suggestions that the authors should take into consideration.

1. The abstract should be written in a more concise way. The inclusion of drug concentrations seems to be too tedious for an Abstract.
2. Similar results have been published and cited in the manuscript (Dineen et al. 2010). It would be nice to make some comparisons between two studies in the Discussion.
3. The significance of the paper could be improved if it were provided with biochemical analysis on mouse tumor tissues.
4. There are some discrepancies in the results from the animal survival experiments (Fig. 6A and 6B.) For instance, for single JP treatments, the survival time was 28 d for Fig. 6B, but 21d for Fig. 6B. What caused the large variability?
5. Although Annexin V staining showed that GEM had an effect on early apoptosis (Fig. 2A), the PARP-1 cleavage experiment did not detect any cleaved PARP-1 (Fig. 2B). Please provide an explanation on this. In addition, a loading control for Fig. 2B could be helpful.

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.