Reviewer's report

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

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Reviewer: Masaaki Tamura

Reviewer's report:

Awasthi, et al. have investigated the efficacy of a Smac mimetic JP1201, a small inhibitor molecule of inhibitors of apoptosis proteins (IAPs), in combinational use with typical chemotherapeutics on pancreatic ductal adenocarcinoma (PDAC) in vitro and in vivo. They found that JP1201 in combination with gemcitabine, doxorubicin, or decataxel additively attenuates the proliferation of pancreatic cancer cells by increasing apoptosis in vitro. They also found that these combination treatments significantly attenuated tumor size and increased mouse survival. Based on these results they concluded that JP1201 augments antitumor effects of standard chemotherapy agents in experimental PDAC.

The basic idea is right, the approach to this subject is acceptable and conducted well, and the results support previous findings. However, recently a similar paper using the same Smac mimetic has been published. In addition, a few other papers utilizing identical rationale but a different chemical have also been published within the last a few years. Although the conclusion from this study is identical to other papers, this paper clearly indicates that a combinational treatment of JP with gemcitibine significantly decreased orthotopic tumor size. This appears to be a good finding. However, this finding was supported by a mouse study with a minimal number of mice (3-4 mice). If the authors respond to the following comments and concerns, the quality of this paper would improve.

Major Compulsory Revisions:

1. The most critical study (Fig. 5) was conducted with a very small number of mice. This is the crucial weakness of this paper. If the authors could repeat the same experiment using at least 6-7 mice per group and obtain identical results, this would be meaningful.

Minor Essential Revisions:
1. For the Western blot analysis (Figs. 2B and 4), loading control such as actin or GAPDH is generally presented. It is difficult to evaluate if higher expression is indeed due to high protein expression or larger amount of sample application without a loading control.

2. There are several typographical spacing problems at scattered places throughout the manuscript.


Level of interest: These findings are mainly confirmatory and are suggestive for a practical clinical application of the Smac mimetic.

Quality of written English: Acceptable

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

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.

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