Reviewer's report

Title: Aberrant Cancer Cell Selectivity in Apoptosis Induction by truncated Apoptin Lacking the Upstream of Leucine Rich Stretch

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Reviewer: Laura Gatti

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COMMENTS FOR THE AUTHORS

Apoptin is a non-structural viral protein encoded by VP3 gene of chicken anemia virus, that could specially induce apoptosis of tumor cells, but shows little or no cytotoxicity in normal cells. In addition, Apoptin shows different localization in tumor cells and normal cells: it predominantly accumulates in nucleus of tumor cells, whereas in normal cells, it is detected mainly in cytoplasm. However, the mechanism of apoptin-induced apoptosis in tumor cells without any side effects in normal cells has not yet been well characterized. The authors of the present study hypothesize that the presence of a minimal selective domain, spanning amino acids 1-31 of Apoptin, is critical for the selectivity in apoptosis induction of cancer cells.

Although the preliminary hypothesis of the present paper could be of some interest, the study has some evident weaknesses, related to the following specific issues:

1. Major Compulsory Revisions

• Since the aim of the authors appears to be the investigation of apoptotic death induced by different truncated Apoptin proteins, they could at least include a better quantitative assessment of apoptosis. Apoptosis should be determined by more conventional and reliable quantitative assays. The authors justify themselves “due to the nature of the experiments which required individual protein injection into each cell, thereby the number of investigated cells was not permissive for quantitative measurement” (Page 14). Is the protein microinjection the better way to selectively deliver Apoptin into normal/cancer cells? Authors are invited to discuss such a point.

2. Minor Essential Revisions

• Reference section need to be updated, including the most important papers on the subject, which have been recently published (e.g., Zhang M, Int J Oncol. 2013; Yuan L, Tumour Biol. 2013; Taebunpakul P Apoptosis 2012; Zhou S Med Oncol. 2012, etc).

• The quality of written English is not acceptable in the present form. The manuscript should be revised by a native English speaker because it needs some language correction before being published.
3. Discretionary Revisions

- The authors are invited to discuss the potential development of a “protein drug” that could have applications in anticancer therapy, since the evidence of several major problems, including poor expression and poor protein solubility of recombinant Apoptin, have hampered until now the efficient production of an engineered protein (Lee MS et al., BMC Biotechnol. 2012).

**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