Reviewer’s report

Title: NF-kappaB targeting by way of IKK inhibition sensitizes lung cancer cells to adenovirus delivery of TRAIL

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Reviewer: Zi-Chun Hua

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The present manuscript tried to test combinatorial gene therapy modality of adenovirus delivery of TRAIL (Ad5hTRAIL) and IKK inhibition (AdIKK#KA) to overcome TRAIL resistance in lung cancer cells. Luciferase assays were used to monitor the regulation of NF-#B activity. The results showed that combination treatment with Ad5hTRAIL and AdIKK#KA induced significant apoptosis of TRAIL-resistant A549 cells, and this may suggest that dual gene therapy strategy of exogenous TRAIL gene expression together with concurrent IKK inhibition may be a promising novel gene. This paper is well written and the results look clear. But there are some scientific defects as follows. It is not qualified for publishing in this journal in its current version. It needs major compulsory revisions

1. The authors did not provide any direct data to show the expression of TRAIL and IKK#KA after gene therapy into cell line, and their respective expression during the combinational therapy modality. There are more parameters which could influence the apoptosis, for example, stress response during protein over-expression may also affect apoptosis.

2. Annxin V can detect the early stage of apoptosis and the authors had better also use one more assay to further demonstrate apoptosis such as activation of caspases.

3. To further confirm the design of the combinational gene therapy modality of TRAIL and IKK#KA, the authors had better add more data to demonstrate the inability of NF-#B’s translocation into the nucleus and also phosphorylation status of IkB.

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.

Declaration of competing interests:

'I declare that I have no competing interests' below