Reviewer's report

Title: Cisplatin sensitivity is enhanced in non-small cell lung cancer cells by regulating epithelial-mesenchymal transition through inhibition of eukaryotic translation initiation factor 5A2

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Reviewer: Stefan Balabanov

Reviewer's report:

This manuscript contributed by Xu et al. is about the role of the eukaryotic initiation factor 5A2 (eIF5A2) in cisplatin response of non-small cell lung cancer cells in vitro. Using a siRNA mediate knock down of eIF5A2 and a pharmacological inhibition of DHS mediated first step of the hypusine modification the authors analyzed cisplatin sensitivity and epithelial-mesenchymal transition (EMT) in non-small cell lung cancer cells in vitro. Xu et al. demonstrate that GC7 treatment enhanced cisplatin induced sensitivity and affected EMT in NCI-H1299 and A549 cells.

General points:

The observations reported in this manuscript are technically well done, interesting and provide novel information how the hypusine modification system, particularly eIF5A2, affects chemotherapy sensitivity and EMT in non-small cell lung cancer cells in vitro. Nevertheless, there are two major concerns, which have to be clarified before further consideration:

Major Revision:

1. The authors are providing data that GC7 is able to enhance the sensitivity of NSCLC cells to cisplatin. Furthermore, they have shown that GC7 treatment affects EMT in NSCLC cells. Based on additional experiments using siRNA against eIF5A2 the authors claim that GC7 effects are due to a specific inhibition of eIF5A2. Since eIF5A1 is expressed in these cells and probably inactivated by GC7 as well, authors have to show that the observed effects are really specifically induced by inactivation of eIF5A2 and are not, at less in part, based on parallel inactivation of eIF5A1. These can be performed by an isoform-specific siRNA mediated knockdown of eIF5A1. Without these additional experiments it is not possible to clearly separate between GC7 mediated eIF51- and eIF5A2-effects. Furthermore, data showing evidences for an inhibition of hypusine modification (e.g. 2-dimensional Western blot analysis) of eIF5A2 compared to eIF5A1 are missing. Those data could strengthen the conclusion that eIF5A2 is the key mediator for the GC7 mediated effects.

So far, the statement: “Cisplatin sensitivity is enhanced in non-small cell lung cancer cells by regulating epithelial-mesenchymal transition through inhibition of eukaryotic translation initiation factor 5A2” is not entirely supported by the data
presented in the current form of the manuscript.

2. The authors have already nicely published a manuscript about “Down-regulation of eIF5A-2 prevents epithelial-mesenchymal transition in non-small-cell lung cancer cells” in 2013 (J Zhejiang Univ Sci B. 2013 Jun;14(6):460-7. doi: 10.1631/jzus.B1200200). In that work, which is online accessible, the authors focused on just one non-small cell lung cancer cell line (A549 cells) and have already shown that a siRNA mediated knockdown of eIF5A2 affects different aspects of EMT in this particular cell line. Even if the new manuscript provides many new experiments (including a second cell line, GC7 and cisplatin treatment) it is mandatory that the authors refer to the former publication. Furthermore, the author should clearly discuss what is different between both publications and whether there might be overlaps between both manuscripts.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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.