Reviewer's report

Title: Gli promotes tumor progression through regulating epithelial-mesenchymal transition in non–small-cell lung cancer

Version: 0 Date: 27 Oct 2019

Reviewer: Zerui Zhao

Reviewer's report:

The work by Jiang et al. investigates the role of Gli transcription factors in inducing EMT in non-small-cell-lung cancer. In this work the authors correlate Gli expression with markers of EMT and biological features alteration following the manipulation Gli-inhibition in NSCLC cells.

Though well-constructed, the following issues in the manuscript need to be addressed.

Major:

1. For the in vivo analysis, the authors describe the percentage of positiveness for each marker without exploring the possible correlation between variables analyzed. For example, the authors indicated that 61.1% (22/36) of tumor samples add Gli1 overexpression over normal counterpart, while 77.8% (28/36) had a similar trend for NCAD. Is there a positive correlation between NCAD and Gli expression in these samples? the same for the other markers analyzed. Adding this information will allow a more stringent correlation between gli expression and EMT markers.

2. The authors use siRNA against Gli1 and 2 showing changes in the EMT markers profile in two different NSCLC cell lines. A recent work by Manzotti et al (Clinical Cancer Research) showed that H1299 cell line has a more mesenchymal-like phenotype as compared with H1975 used in this manuscript. This cell line, being gone further in the EMT process, may hence represent a more reliable cell model to test Gli effect on EMT. The authors may also want to discuss this work in their discussion.

3. The authors posted background information in the introduction section to introduce the rationale of their work. However, some contents are suggested to be placed in the discussion section for making the first part of your article succinct.

Minor:

1. I would suggest using "epithelial-mesenchymal transition" instead of the abbreviation "EMT" directly in the title.
2. It would be better to mention GANT61 as the selective inhibitor of Gli transcription in the Hedgehog pathway in the first place.

3. Forty references were cited at the end of the discussion, however, only 30 of them were listed in the manuscript. Please make sure all references are cited in a proper manner.

**Level of interest**
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