Peer Review File

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Reviewer A

1. This research focused on LncRNA HOXD-AS2 regulates miR-3681-5p/DCP1A axis to promote the progression of non-small cell lung cancer, after check the pubmed, no related articles, this mauscript was more comprehensive and specific.

Reply 1: Thank you for your affirmation. We will try our best to make more contributions to this area.

2. Only 2 authors to finish so much scientific targets, as hosipitals doctors it was so hard work.

Reply 2: Thank you for your comprehension. We are happy that we can finish this work. Thanks so much.

3. Where did you do the Xenograft tumor models? Because raising nude mice requires special environment and qualification.

Reply 3: Thank you for your question. Xenograft tumor models were experimented in the laboratory animal center of Nanjing Agricultural University.

Changes in the text: We have modified our text as advised (see Page 8, line 249).

4. The statistical software version is too low and the the statistical method is not very detailed.

Reply 4: Thank you for your question. The statistical software version is the one commonly used and we have added more details of the statistical methods in this paper.

Changes in the text: We have modified our text as advised (see Page 9, line 293 and 295).

5. Although you have done the tumor model, why not to observe the OS and the relationship with the studied gene.

Reply 5: Thank you for your proposal. The current paper mainly focused on the fundamental research in NSCLC, thus observation of OS and relationship with studied gene are considered to be explored in future study. We are so sorry that we have no enough time to do these researches now. Thanks so much.

Changes in the text: We have modified our text as advised (see Page 14, line 447 and 448).

6. English need to further perfect.

Reply 6: Thank you for your advice. Our manuscript has been edited with the help of English Language Editor: J. Jones. There may be some mistakes caused by misunderstanding. We have read the whole manuscript and tried our best to make the sentences more readable in the revised manuscript. Thanks so much.

Changes in the text: We have modified our text as advised (see Page 2-13, line 41 to 430).

Reviewer B

LncRNA HOXD-AS2 regulates miR-3681-5p/DCP1A axis to promote the progression of non-small cell lung cancer by Zhang et al

I found, that the topic is original and relevant in the field.
I found the conclusion to be in line with the evidence and arguments presented.
The references are well-updated.
The Figures are of good quality.
The manuscript is interesting, however, it can be improved and strengthened by addressing the following comments -
Minor points:

An important study is missing (PMID: 35327612). Authors should cite this study in the introduction section.
Reply 1: Thank you for your reminding. We have cited this study (reference 12) in Introduction part.
Changes in the text: We have modified our text as advised (see Page 3, line 76).
The Caption of Figure 2 is not clear.
Reply 2: Thank you for your advice. We have supplemented the explanation of Figure 2.
Changes in the text: We have modified our text as advised (see Page 19, line 598-602 and Page 20, line 603).
Overall nice work!!

Reviewer C

The paper titled "LncRNA HOXD-AS2 regulates miR-3681-5p/DCP1A axis to promote the progression of non-small cell lung cancer" is interesting. HOXD-AS2 modulates the miR-3681-5p/DCP1A axis to boost the progression of NSCLC, which founds the basis of HOXD-AS2 as a new diagnostic biomarker and molecular target for NSCLC therapy. However, there are several minor issues that if addressed would significantly improve the manuscript.

1) There are many lncRNA that regulate the progression of NSCLC. Why did the author choose lncRNA HOXD-AS2 for research? Please describe the reason.

   Reply: Thank you for your suggestion. In our research, GSE138172 dataset has analyzed the overexpression of HOXD-AS2 in NSCLC tissues compared with normal tissues. As an oncogenic lncRNA, HOXD-AS2 has been proved to be heightened in glioma. We hypothesized that HOXD-AS2 may also participate in the progression of NSCLC. Thus,

lncRNA HOXD-AS2 was selected for research.

Changes in the text: We have modified our text as advised (see Page 12, line 397-401).

2) What is the impact of this study on the further treatment and prognosis of NSCLC? It is recommended to include relevant content in the discussion.

Reply: Thank you for your advice. This study may provide a optional molecular target and diagnostic marker for further treatment and prognosis of NSCLC patients.

Changes in the text: We have modified our text (see Page 13, line 432-433).

3) What are the potential relationships between lncRNA HOXD-AS2, and epithelial-mesenchymal transition? How interaction of these processes may affect NSCLC progression, chemoresistance and ultimately recurrence? It is recommended to add relevant content.

Reply: Thank you for your recommendation. Our manuscript mainly focused on the effect of HOXD-AS2 on cell proliferation, migration, invasion and apoptosis. Thus, we plan to interrogate the potential relationships between HOXD-AS2 and epithelial-mesenchymal transition, chemoresistance and ultimately recurrence in future studies. This is also the limitation of our paper.

Changes in the text: We have modified our text (see Page 13, line 436-439).

4) The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as "LncRNA OXCT1-AS1 promotes the proliferation of non-small cell lung cancer cells by targeting the miR-195/CCNE1 axis, PMID: 35706791", "LncRNA B4GALT1-AS1 promotes non-small cell lung cancer cell growth via increasing ZEB1 level by sponging miR-144-3p, PMID: 35402178". It is recommended to quote the articles.

Reply: Thank you for your advice. We have quoted the articles to make the introduction part more comprehensive.

Changes in the text: We have modified our text as advised (see Page 3, line 77-79).

5) Can lncRNA HOXD-AS2 be used as a potential biomarker for patient risk stratification and local regional metastasis in NSCLC? It is recommended to add relevant content.

Reply: Thank you for your recommendation. Our current study mainly focused on fundamental research in NSCLC, not involving deep clinical studies. Thus, the potential of HOXD-AS2 as a potential biomarker for patient risk stratification and local regional metastasis in NSCLC could be investigated in in-depth researches.

Changes in the text: We have modified our text (see Page 13, line 439-440).

6) Does the ceRNA regulatory network in this study affect the radioresistance of NSCLC? What impact might it have? It is recommended to add relevant contents.

Reply: Thank you for your recommendation. Radioresistance is also an consideration for the effect of the ceRNA regulatory network in NSCLC, however, in the present research, we aimed to explore the influence of HOXD-AS2 on basic cellular activities, such as proliferation, migration, invasion and apoptosis. Hence, future study will focus on the impact of the ceRNA regulatory network on the radioresistance of NSCLC.

Changes in the text: We have modified our text (see Page 13, line 438).

7) What are the problems and challenges that need to be overcome in the clinical application of lncRNA? It is recommended to add relevant content.

Reply: Thank you for your reminding. More NSCLC specimens and characteristics of NSCLC patients should be collected for analyzing the clinical application of lncRNA.

Changes in the text: We have modified our text as advised (see Page 13, line 440 and Page 14, line 441-442).

Reviewer D

1. ARRIVE checklist:

Blinding method was not described in main text of your paper, please supplement it in Methods section of the main text and fill Section/Line number in this item; or you could just fill "N/A".

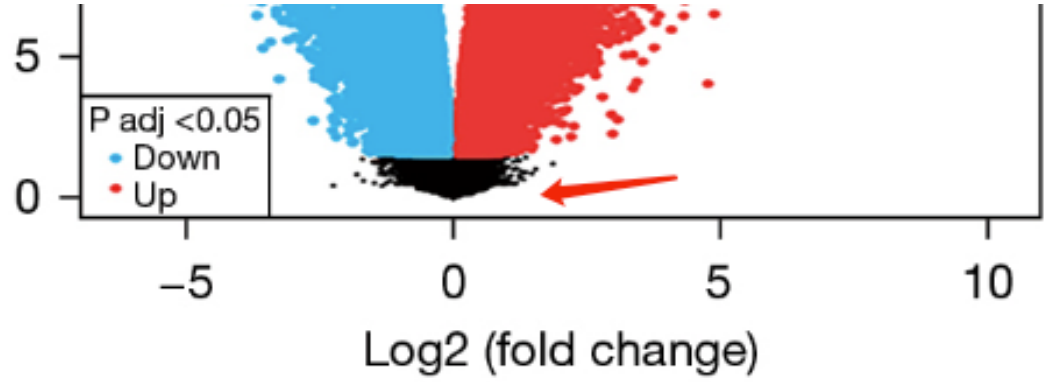
Blinding	5	Describe who was aware of the group allocation at the different stages of the experiment (during the allocation, the conduct of the experiment, the outcome assessment, and the data analysis).	The first and corresponding author are aware of the specific implementation.

Answer: Thank you for your advice. We supplemented N/A in the item of Blinding.

2. There're two references lists included in your paper, please keep the final version and remove the unnecessary one.

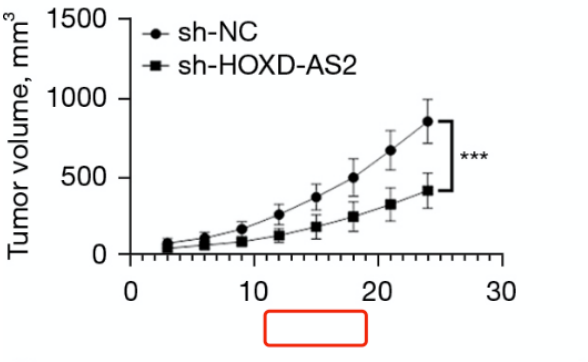
Answer: Thank you for your reminding. We have deleted one references list.

3. Figure 1: Please also define those black dots either inside the figure or in figure legends,



Answer: Thank you for your suggestion. We have explained black dots in figure legends of Figure 1A.

4. Figure 5A: Check if description is missing for X-axis in this figure.



Answer: Thank you for your suggestion. We have added the explanation for X-axis in this Figure 5A.