Peer Review File
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Reviewer A

This study investigated expression pattern of LOXL family in squamous cell lung cancer (LUSC), and found overexpression of LOXL 1 and 2 mRNA. Especially, LOXL2 was correlated in poor prognosis of LUSC. In vitro experiments, knockdown and inhibition of LOXL2 resulted in suppression of progression, migration and invasion of LUSC cell lines.
I could not find any problems in the study method. The results contained some novelty.

However, some minor comments need to be addressed.

Minor Comment 1. Generally, male and smoker are prone to LUSC. Non-smoker rarely develops LUSC. How many male and smoker patients were enrolled in the analyses of Fig 1 and Table 1.
Reply 1: 371 males and 472 smokers were enrolled in the analyses of Fig 1 and Table 1 (see page 7, line 227).

Minor Comment 2. Despite of the second study limitation described in Discussion, can the authors show the immune-histochemical staining of cancer and surrounding non-cancer areas by LOXL1 and 2? Although the graphs of Fig 1A and B show that LOXL1 and 2 were more highly expressed in cancer than in normal and non-cancer, these gene expression were not so specific only in cancer. Can this expression difference can be demonstrated by immunohistochemical staining in the cancer and non-cancer tissue?
Reply 2: We agree with the reviewer's comment. Unfortunately, we do not have specimens from patients with LUSC now and therefore cannot perform immunohistochemical testing. However, we will further validate the relationship between LOXLs expression and LUSC prognosis clinically, and we will collect LUSC specimens and perform immunohistochemical staining to detect LOXLs expression.

Minor Comment 3. The authors should describe the selection criteria of the independent variables in Table 2 from the univariate to the multivariate analyses.
Reply 3: We agree with the reviewer's comment. If the p value in the univariate analysis was less than 0.1, the variable would be included in the multivariate Cox

regression analysis. (see Page 7, line 217-218)

Minor Comment 4. In Discussion, page 10, the second paragraph, 'The results suggested that upregulation of LOXL1 and2 may be involved in tumorigenesis rather than progression'; These clinical data were not consistent with the results of the later in vitro experiments, showing that downregulation of LOXL2 suppressed progression, migration and invasion. The authors should describe these discrepancy between clinical data and in vitro experimental results.

Reply 4: In human body, in addition to oncogenes and oncogenes, tumor development is affected by many other factors, such as the immune system, lipid metabolism, tumor microenvironment and so on. The in vitro experiments only examined the effects of LOXL1 and LOXL2 on tumor cells, and did not examine the effects of other factors (Page 12, line 372-376).

Minor Comment 5. For what was LOXL1 overexpressed? In this study, LOXL2 was overexpressed in LUSC, and involved in tumor progression and poor prognosis. Can the authors speculate the role of LOXL1 in LUSC?

Reply 5: It has been pointed out that overexpression of integrin α11 increased LOXL1 expression in non-small cell lung cancer and promotes tumor growth and progression. LOXL1 induces NSCLC cell invasion by affecting collagen matrix remodeling. In addition, LOXL1 is associated with chemotherapy resistance in NSCLC. (Page 11, line 340-344)

Reviewer B

With a few improvements, your manuscript can reach its full potential.
1: the introduction needs to provide a comprehensive transition between discussing NSCLC and introducing LOXL, ensuring a smoother flow between these topics.

Reply 1: We have revised the introduction section (Page 4, line 101-103).

2: Remove the statistical details from the introduction part and replace them in the analysis part

Reply 2: We have revised the introduction part and analysis part (Page 4, line 108-112; Page 7, line 214-215, line 217-218).

3: In the result part, give the survival rates or median values with high vs low LOXL2 expression.

Reply 3: We have revised the result part (Page 8, line 265-269).

4: line 291, it would be beneficial to explicitly state the study's key findings before delving into the discussion of LOXL proteins.
Reply 4: We have revised the discussion part (Page 10, line 328-330).

5: in the conclusion part, state the potential implications of the study findings on clinical practice and future research.
Reply 5: We have revised the conclusion part (Page 13, line 402-406).

Overall, the article comprehensively investigates the expression pattern and prognostic value of LOXL1 and LOXL2 in lung squamous cell carcinoma. The use of bioinformatic methods, high-throughput sequencing, and genomic microarray technology lends strength to the study.