

Peer Review File

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Reviewer A

My major concerns:

1. The logic and structure of the paper are very confusing. It is hard to tell the relationship between the parts and why the authors listing the parts in such order.

REPLY 1: Dear reviewer, thank you very much for your observations. They are highly appreciated. The authors wish to clarify that they discussed three promising treatment strategies for lung squamous cell carcinoma: **lncRNAs as biomarkers in LUSC, Immunotherapy in LUSC, and DNA methylation in LUSC**. These treatment strategies were separately discussed. Hence, the structure of the paper. Structurally, we firstly discussed lncRNAs in cancer and mechanisms of action, lncRNAs in lung cancer, and lncRNAs in LUSC. Also, we discussed immunotherapy in lung cancer and immunotherapy in LUSC, and lastly, we discussed DNA methylation in LUSC.

However, based on your valuable observations, we have revised the structure and parts of the paper. Please see **page 9, line 205, page 10, line 231, page 11, line 240, page 13, line 301, page 18, line 376, page 20, line 424, page 23, line 490, page 25-26, lines 525, 538, 565, and page 28, line 591**

2. There are many duplicates among the different parts, like instruction and its following part.

REPLY 2: Thank you once again for flagging this out. According to your observations, we have revised the manuscript by removing duplicates wherever they were found. Please see **page 32, line 704-706, page 39, line 838-841, line 855-856, page 36, line 787-788, page 33, line 708-712**.

We also revised some headings and subheadings in the manuscript; please see

page 10, line 231, page 11, line 240, page 13, line 301, page 18, line 376, page 20, line 424, page 23, line 490, page 25, line 525, page 28, line 591.

Moreover, we have added some information to the manuscript. Please see, **page 9, line 205-230, page 11, line 237-239, line 242-248, page 13, 14, line 302-307, page 19, line 405-411, page 36, line 790-793.**

Also, there were some structural changes made to some sentences and paragraphs in the manuscript. Please see, **page 4, line 89-92, page 12, line 259-264, line 278-284, page 15, line 346-361, page 18, line 385-388, page 21, line 449-453, page 22, line 482-485, page 23, line 501-503, page 28, line 603-608.**

3. So many paragraphs are focused on other cancers or diseases, not LUSC.

REPLY 3: Dear respectful reviewer, thank you again for raising the point out. We would have so dearly love for you to indicate that portion of the manuscript that is focused on other cancers. However, we have reviewed the manuscript and noticed that the portion with the heading “the role of lncRNA in cancer and mechanisms of action” (**page 6, line 121**) discussed other cancers instead of LUSC. The authors will like to clarify that they inserted the portion mentioned above to give the reader a general knowledge of lncRNAs in different cancers before reading about LUSC, one of the different types of cancer.

My minor concerns:

1. Paragraph from line 268 is focused on diagnostic marker, why not put in the following part.

REPLY 1: Dear reviewer, after your valuable advice, we have put paragraph 268 into the following part that reads, “lncRNAs as diagnostic and prognostic biomarkers in LUSC”. Please see **Page 21, Line 454-457.**

2. Some annotation should be added to the abbreviations first showed, like OS rate in line 297, PCa in line 318.

REPLY 2: Dear reviewer, thank you again for your valuable suggestions and comments. In line with what you have suggested, we have annotated abbreviated words firstly mentioned in the manuscript. **Please see page 3, line 70-71, page 16, line 364, page 20 line 436, page 21, line 462, page 24 line 519-520, page 30, line 654.** Moreover, we have annotated almost all abbreviated words mentioned in the manuscript. Please see pages **41-45**

3. Is there a table for lncRNA acting as oncogenes in LUSC?

REPLY 3: Thank you again for highlighting this missing portion in our manuscript. We provided a table containing a list of lncRNAs and their functions in lung squamous cell carcinoma, but we did not mention their role as oncogenes or tumor-suppressors during our first submission. Based on your question, we have modified our table by indicating the role of lncRNAs as either oncogenic or tumor-suppressive in lung squamous cell carcinoma. Please see **table 1** with the heading “**oncogenic and tumor-suppressive roles of lncRNAs in LUSC**”. Additionally, in the manuscript, we subdivided and separately discussed lncRNAs as oncogenes and as tumor-suppressors in lung squamous cell carcinoma. Please see **pages 10-16**

Reviewer B

1. Some cons of lncRNA for lc should be discussed, as well as the language required polishing

REPLY 1: Dear reviewer, thank you very much for your kind suggestion. We believe it is in the best interest of helping to make our manuscript better. Based on your valuable advice, we have added in the text a portion with the subtitle: “**lncRNAs in lung cancer,**” which contains some functional roles of lncRNAs in lung cancer. Please see **page 9, Line 205-230**. Additionally, we subdivided and separately discussed lncRNAs as oncogenes and as tumor-suppressors in lung squamous cell carcinoma. Please see **pages 10-16, and table 1**.

Additionally, we submitted to your advice in terms of language polishing by

making some grammatical corrections in the entire manuscript where necessary.

Please see the **manuscript with highlighted grammatical corrections**.