Reviewer’s report

Title: Integrative analysis of genetic and epigenetic profiling of lung squamous cell carcinoma (LSCC) patients to identify smoking level relevant biomarkers

Version: 0 Date: 24 Jun 2019

Reviewer: Shijie Zheng

Reviewer's report:

The authors tried using both of RNA-seq and DNA methylation from TCGA LSCC dataset to identify smoking associated biomarkers. However, I could hardly find new exciting biological insight in this research.

Detailed comments:

1. The TCGA DNA methylation data of LSCC is not seq-based profiles. The samples were profiled using Illumina 450K beadarray. The author should methylation instead of methyl-seq.

2. There is a typo in the formula to calculate the p value of enrichment.

3. As shown by the PCA on expression profiles, the dichotomized smoking levels were not correlated with the top two PCs. Then, the question is what is driving the variation. The author could identify the source and include the source as covariate in the following analyses.

4. The authors could look into the smoking pack years more carefully. Some demographic summary should be provided. In this particular case, gender might be a confounding factor to smoking groups. Are genders balanced between to smoking groups? If not, the differential analyses might give us differentially expressed genes or differentially methylated CpGs between genders.

5. For the integrative analysis, how the author defined the gene and CpG site pair needs to be further illustrated. Was it based on PCC, R2, or p value of correlation test?

Level of interest
Please indicate how interesting you found the manuscript:

An article of limited interest

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published
Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal