Peer Review File

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Reviewer A

Cao et al. provide an analysis of alterations in the lipid metabolism that could be associated to the prediction of lung cancer set up. To that end, they screened the differentially expressed genes (DEGs) of lung cancer samples of The Cancer Genome Atlas database. Then, they use the Molecular Signatures Database (MSigDB), the Gene Set Enrichment Analysis (GSEA), and the Gene Card database metabolism-related data to identify those genes involved in lipid metabolism. They use biostatistical analytical tools to identify significant genes related to the risk to develop lung cancer and describe a model with 11 genes related to lipid metabolism as a predictive signature. Finally, the selected signature was used for the prediction of response to commonly used chemotherapy agents by analyzing whether the characteristic model was effective in predicting lung cancer prognosis. The final goal was to provide new tools for lung cancer treatment by identifying novel potential therapeutic targets.

The manuscript does not provide the necessary experimental details to support the author's conclusions. It needs to include additional information to be convincing.

Specific comments:

- Lung cancer is not a unique clinical entity. Authors need to provide additional information on the specific subtype(s) of cancers that have been included in the study. It will be quite surprising that the conclusions of the study could be extrapolated to all lung cancer types.

Reply: we have added additional information on the specific subtype of cancers.

Changes in the text: see Page 2, line 53

- It is difficult to realize what is presented in several of the figures, making it rather arduous to visualize them.

Reply: we can't understand what's the meaning of it.

- The text needs to be checked for misspellings.

Reply: we have corrected the spelling mistakes.

Reviewer B

The manuscript is very interesting, but has several spelling errors. Moreover, several problems need to be solved:

The figures are blurred and incomprehensible; some writings overlap; authors should increase the resolution. All the results and figures need to be explained in more depth, they are too generic.

Line 159: the authors state: "…which were observed from the volcano plot and heatmap, respectively (Figure 1A)" but in Figure 1A there is only a heatmap and not the volcano plot. Please add the missing data.

Reply: we have added the volcano plot.

Changes in the text: see Figure 1.

Figure 1B: what are the genes in common between LUAD and Lipid metabolism? The authors should provide a list of them.

Figure 1C: BP, CC, MF, stay for?

Reply: we have added a list of the genes in common between LUAD and Lipid metabolism and explained BP, CC, MF.

Changes in the text: see Figure 1 and ATTACHED TABLE 1.

Line 170: specify what is meant by "healthy controls".

Reply: normal people without lung cancer.

Changes in the text: see Page 4, line 170

According to which criterion were the patients classified as high or low risk? How many patients are there in each group?

Reply: patients were divided into high risk and low risk according to the median risk score. There are 248 patients at high risk and 249 patients at low risk.

Changes in the text: see Page 4, line 125

How was the sensitivity to the various chemotherapies evaluated?

Reply: the sensitivity to various chemotherapy was evaluated by IC50 value.

Line 308: the authors state: "…indicating that cases displaying high-risk scores showed high chemosensitivity". This sentence implies the opposite of what is shown in Figure 5.

Reply: the ordinate of Figure 5 shows the IC50 values of various chemotherapy drugs, and the lower the IC50 value, the more sensitive the group is to chemotherapy drugs.

Changes in the text: see Figure 5