Reviewer’s report

Title: Multiplex plasma protein profiling identifies novel markers to discriminate patients with adenocarcinoma of the lung

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Reviewer: Ping-Li Sun

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My specific comments are as follows:

1. The manuscript was relatively well written, but the clinical significant is not so great, Is this method is practical and easy to be performed in the routine clinical practice?

2. And the clinical significance of screening early stage lung cancer will be prominent than advanced stage lung cancer, because the clinical symptoms are obvious in these patients. And this study did not stratify the patients to early stage and advanced stage.

3. Because of the implementation of routine physical examination, the lose dose CT still the best screening method to find lung cancer, especially for early stage diseases, in fact, the problem that needs to be solved urgently is the discrimination of non-malignant disease, such as tuberculosis, and inflammatory diseases, so I recommend the study design should focus on the non-malignant disease whose CT features is hard to distinguish from lung cancer, to find the different blood plasm biomarkers.

4. Some of the carcinoma patients also showed inflammation, especially the central type, when cause the obstruction of lung bronchial, so the inclusion and exclusion criterias of the study cases should be carefully designed. If some cases of the LCA patients has the combination of lung inflammation?

5. And in the further study, the validated study in the cell lines and clinical patients should better be considered.

6. This is a retrospective study, in the study of screening new biomarkers, the perspective study should be performed.

7. More study should be done, especially the literature review about the functions and expressions of these different proteins in the lung cancer and other non-malignant diseases.

8. The histologic type of the lung CRC met should better be given, and dose the LCA group include the mucinous, enteric or colloid type carcinoma? Because these types of cancer may share the similar protein profiles due to the overlap of the histologic features.
9. Also are all the carcinoid tumors origin from lung or colon?

10. What means semi-malignant?

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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

Acceptable

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