Peer Review File

Reviewer A

I am unconvinced by the conclusions drawn from these data.

More explanation required as to the cohorts the differentially expressed gene data were drawn from i.e. inclusion criteria, heterogeneity, where genetic material was taken from, e.g. blood? respiratory samples? Significant heterogeneity may limit the validity of any data drawn from these samples.

I appreciate the heterogeneity between 2 chips and related inconsistencies, but am unclear why only downregulated genes were looked at. Does this not mean that the relevant data is looking at genes and pathways that are switched off in CAP?

It is unclear why 'melodysplastic syndrome' was used as a search term to look for genes related to CAP.

I am surprised as to the very few genes that were defined as candidate genes relevant to CAP once all the data were analysed. Given the complex host-pathogen interactions and multiple immune and inflammatory pathways identified in the literature, it is unexpected that only 4 items of significance were found. There is no obvious involvement of innate immune system pathways which is very surprising, and makes me question the validity of the approach or analysis used.

It would have been more informative to look at IL7R in CAP patients v non CAP patients. Also IL7R expression values compared to organism, rather than low v high expression would have been more informative. It would also be more valuable to assess IL7R related to patient outcome if the eventual aim is translational for either diagnostic or therapeutic purposes.

As a result the conclusions as to importance of IL7R are an extrapolation too far from the data reported.

I'm confused as to line 307, surely the aetiology of CAP is pathogen-dependent.

Minor point:

Some of lines 252-261 should be moved to the relevant figure legend

Answer: Thank you for your careful guidance. In our article research, we utilized information from public databases for bioinformatics research. During the analysis process, we analyzed the healthy population and the CAP population for comparative analysis, and used mathematical processing to reduce the impact of heterogeneity between the two data, achieving the best state we can currently achieve. At the same time, we reviewed our clinical data based on the content of bioinformatics analysis, We conducted a retrospective analysis and explored the data, and it is possible that our relatively simple bioinformatics analysis method is not yet perfect.

The involvement of IL-7R gene in severe CAP was already known (Ampuero S, et al. Sci Rep 2022; 12: 13145), but the present study doesn't add any finding of clinical usefulness.

Answer: Thank you for your careful guidance. This article is a retrospective analysis of the relationship between clinical data analysis molecules and the tendency of pathogenic bacteria to occur from the perspective of bioinformatics analysis, and is not specific to this molecular research. Improvements will be made to address the shortcomings of the article

Community-acquired pneumonia (CAP) refers to pneumonia that occurs when the human body is infected with bacteria, fungi, viruses, or mixed infections outside the hospital or in the community environment. CAP is a common infectious disease that threatens human health. In the manuscript "Prediction of target genes in community-acquired pneumonia based on the bioinformatics method", authors used bioinformatics analysis methods to explore the differentially expressed genes (DEGs) of CAP, the disease-related signaling pathways, and the protein-protein interaction (PPI) network to predict the relevant genes that may play an important role in the progression of CAP at the molecular level and revealed the molecular mechanism of CAP.

Couple questions are required to be answered before it will be accepted.

1) In the title page, "Huaian" and "Huai'an" both were showed. Please unify. In the abstract, the background of abstract was not suitable. Please revise.

Answer: Thank you for your careful guidance. We have corrected and unified the expression of Huai'an. At the same time, the background content of the abstract section of the article has been revised based on the review comments.
Change in the text: Page 2/line 54-57.

2) What was the meaning of "NOM (Nominal)" and "gene set enrichment analysis (GSEA) was used to explore the relationship between CAP and NOM (Nominal) P<0.05 is the standard KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway and core gene"? please state clearly.

Answer: Thank you for your careful guidance. Based on the review comments, the content of this section of the article has been revised and clarified."Simultaneously, gene set enrichment analysis (GSEA) was used to explore the KEGG pathway and core genes related to CAP. The screening criteria for significant pathways were NOM p-val<0.05 and FDR (qvalue)<0.25."
Change in the text: Page 2/line 61-64.

3) It was better to add related reference (DOI: 10.21037/arh.2017.05.02) about the review of community-acquired pneumonia.

Answer: Thank you for your careful guidance. We have added the related reference (DOI: 10.21037/arh.2017.05.02) to the introduction.
Change in the text: Reference 3.

4) In the study, why only to focus on the downregulated DEGs? Please state in the part of results. In the whole text, "alveolar lavage fluid" should be changed to "bronchial-alveolar lavage fluid (BALF)". Please state clearly the methods of immunohistochemistry of BALF in the part of methods. And provide representative images of BALF in the part of results.

Answer: Thank you for your careful guidance.   After analyzing the data, the author of this article found some correlation between the downregulated dataset and clinical data, and therefore presented the corresponding results. We have changed "alveolar lavage fluid" to "bronchial-alveolar lavage fluid (BALF)". And We have supplemented the steps of the immunohistochemistry experiment, but the image was lost due to a computer problem at the research institute. We apologize for not being able to provide this information.
Change in the text: Page 7/line 228-237.

5) In the study, the IL7R was the key gene. It was better to validate the expression of IL7R by experiments.

Answer: Thank you for your careful guidance. Due to experimental funding and other objective constraints, further experimental verification will be conducted in future research.
Change in the text: None.

6) In the part of "Screening of DEGs by GSEA", "This finding may inform our cytological research in the future" was stated. Please supplement your cytological research in the future in the discussion.

Answer: Thank you for your careful guidance. At present, this article has not been able to complete the research on cytology experiments. GSEA has predicted some possible mechanisms of action through bioinformatics analysis, but we need to further improve experimental verification in future research.
Change in the text: None.

7) What were the correlations between IL7R and the occurrence of CAP? And what were the roles of IL7R in CAP? Please state in the discussion.

Answer: Thank you for your careful guidance. Regarding the signaling pathways involved in the analysis and prediction of IL7R through bioinformatics, including immune deficiency, T cell receptor signaling pathways, cytokines, and inflammation related pathways, which have been proven to be related to the occurrence and development of CAP in previous studies, we can infer that there is an intrinsic connection. We have provided some explanations in the discussion section. See page 12 /line 378-386.
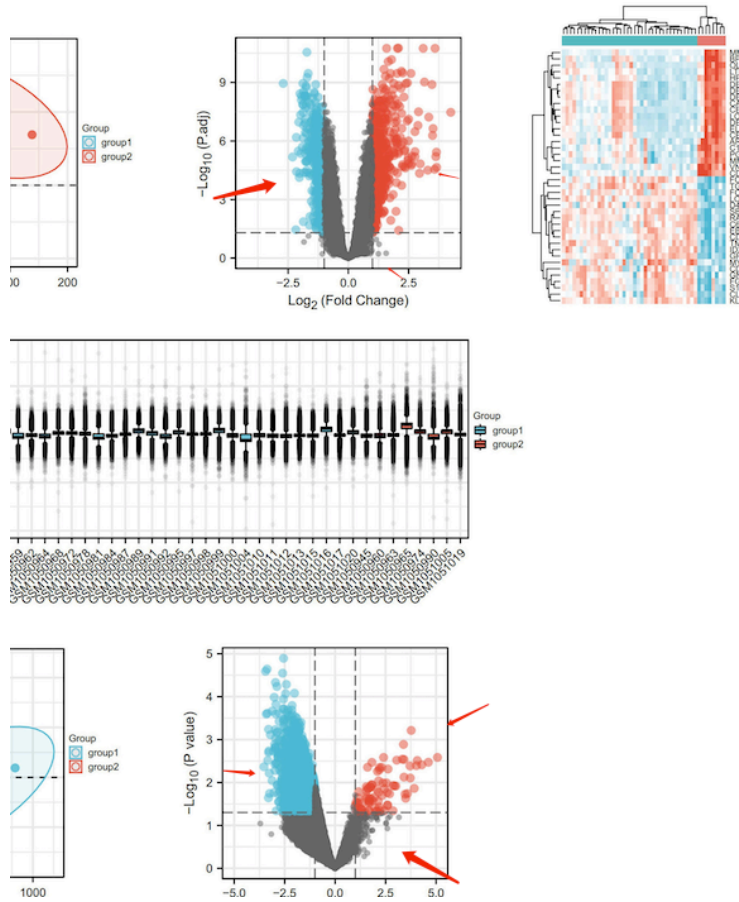
Reviewer D

1. Abstract: Check if "q value" here is correct.

> 62   enrichment analysis (GSEA) was used to explore the KEGG pathway and core genes
> 63   related to CAP. The screening criteria for significant pathways were NOM (Nominal)
> 64   p-val<0.05 and FDR (q value)<0.25. The candidate genes were then intersected with

Reply: Thank you for your comment. "q value" is correct.

2. Figure1A-1B: Please define those blue, red and black dots either inside the figures or in the corresponding figure legends.

3. Please define all abbreviations shown in Figure 4 in its figure legends. Like "NES", "FDR"