

Peer Review File

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Reviewer A:

Comment 1: The abstract section says nothing about the analyses performed on mice and cell lines.

Response: Thanks for your valuable suggestion. We have carefully revised the **Abstract** section and included analyses performed on mice and cell lines (Page 3, line 45-52).

Comment 2: The introduction section lacks specific aim of the study with an explanation of all the research undertaken (lines 91-96 are too scarce).

Response: Thanks for your professional suggestion. We have meticulously revised the **Introduction** section and specifically added the specific aim of the study along with an explanation of all the research undertaken (Page 7-8, line 112-123).

Comment 3: The aim of the work and the specific results should be more focused in the abstract and a clear hypothesis should be elaborated in Introduction section.

Response: Thanks for your valuable advice. Following your suggestions, we have revised the **Abstract** and **Introduction** section (Page 3-4, line 45-61 and Page 8, line 124-126).

Comment 4: There are no information provided for bioinformatics analyses, no links,

no references, no data access for numerous databases: TCGA and GSE data, KM-plotter, CancerSEA database, JASPAR online database, the Animal Transcription Factor Database...

Response: We appreciate your professional suggestion. We have added links to all databases in the revised manuscript.

Comment 5: For the gigantic amount of experiments performed in this study the discussion section is scarce and it does not follow the aim of the study, which was stated by authors as: “to comprehensively evaluate the functions of novel immune-associated genes in the progression and immune microenvironment of lung adenocarcinoma (LUAD)”. Here again the introduction section lacks a specific explanation of the aim of the study and why certain experiments were done. That is why the Results section is rather chaotic and not arranged coherently.

Response: Thanks for your valuable suggestion. According to your advice, we have expanded and revised the **Discussion** section (Page 29-31, Paragraph 3-6). At the same time, we have emphasized a specific explanation of the study's objectives and the reasons behind conducting certain experiments in the **Introduction** section (Page 7-8, line 112-123).

Some minor comments:

Comment 6: LUAD abbreviation should be explained in the first mention not only in abstract but also in introduction (line 63). There is no need to explain abbreviations more than once through manuscript (e.g. TIME as in 67, 92-93).

According to HUGO guidelines all genes names should be italicized, please make

necessary changes through manuscript.

Response: We appreciate your professional advice. Following your suggestions, we have reviewed the entire article and made thorough revisions.

Comment 7: Discrepancy in the number of tissues/patients, why 20 (or 19) of them?1.

Response: We apologize for our unclear description. The data from 19 lung adenocarcinoma samples were derived from previous research conducted at our center, focusing solely on the analysis of ITGB4 expression. This dataset was utilized to supplement our findings on the high expression of ITGB4 in lung adenocarcinoma. The samples from 20 lung adenocarcinoma cases were collected by us from our center for the first time, and we conducted significant immunohistochemistry experiments on these tissues, which are also a central focus of our current study.

Reviewer B:

Comment 1: The overall writing has some formatting issues, like wording, spacing, and some redundancy. I suggest the authors check the grammar and avoid any typos.

Response: We are very sorry for the mistakes. We have reviewed the entire manuscript and corrected the formatting issues in the revised manuscript.

Comment 2: The method part is lack of details. More detailed descriptions are needed to explain the detailed analysis procedures. Provide additional details on the experimental procedures, particularly regarding in vivo experiments and statistical analyses. Ensure consistency in terminology and formatting throughout the manuscript.

Response: Thanks for your valuable advice. We have meticulously revised the entire **materials and methods** section, with particular emphasis on expanding details regarding the experimental procedures and analysis procedures.

Comment 3: The font size in almost every figure is too small. I would recommend the authors to polish figures with high resolution and larger font size.

Response: Thanks for your valuable suggestion. Following your advice, we have increased the font size in all figures. Additionally, we have set the resolution of all figures to the highest level.

Comment 4: There are some similar bioinformatics work revealing biomarkers. I would recommend the authors discuss such work (e.g. PMID: 35173534; PMID: 35151844), which may enhance the current finding in this study.

Response: We appreciate your professional advice. We have carefully reviewed these studies and discussed them in our manuscript's **Discussion** section (Page 31, line 606-612).

Comment 5: Consider discussing potential limitations and future directions of the study to provide a comprehensive overview.

Response: Thanks for your professional advice. As you suggested, we have conducted a detailed discussion on the potential limitations and future directions of the study in **Discussion** section (Page 29, line 562-565 and Page 30, line 594-597). Thank you again for your valuable input.