

## **Respond to reviewers' comments**

### **Reviewer #1:**

**N0. 1: You recruited 151 esophageal cancer patients and 653 healthy controls for this study. I think this study requires IRB approval and informed consent of participants.**

Answer: We thank the reviewers for their attention to ethics and informed consent. I may have misunderstood you due of the unclear expression in the manuscript. Our study does not directly use any people or animals; instead, it is based on information from a public database. It is an additional processing of the previously released data. So, we will be sure to make this point clear in the updated manuscript.

### **Reviewer #2:**

**N0. 1: The abstract of manuscript is too long. Please brief it as you can.**

Answer: I appreciate the reviewer's comments. We completely adhered to the journal's guidelines when we started to refine the abstract's contents and we kept the word count within the allowed range.

**N0. 2: I recommend to check the English of manuscript by a native speaker. There are some problems regarding grammar and article-specific language modification.**

Answer: Thank the reviewer for correcting the manuscript's grammar and spelling mistakes. Based on the reviewer's remarks, we carefully revised the article. Using the QuillBot (<https://quillbot.com/>), we also performed sophisticated polishing. After that, Professor Yu Hua reviewed, checked, and validated that there were no grammatical issues.

**N0. 3: Please simplify the result. The final goal of statistics and result section is transferring results as best way. So, It is necessary to report your finding more simple. I suggest to add a sentence as a non-static result at the end of each paragraph.**

Answer: We completely concur with the reviewer's comments. We added concluding and summary sentences to each section and deleted extraneous and duplicate content in response to the opinions of three reviewers.

**N0. 4: Discussing section is not well-written. Please compare your findings with more studies.**

Answer: I appreciate you pointing up the spelling and grammar error. We extensively revise the article in light of the reviewer's suggestions. We also carry out sophisticated polishing using the QuillBot (<https://quillbot.com/>). Professor Yu Hua review, check, and validate that there are no grammatical issues. The discussion section has certain flaws, but we carefully correct them using the comments provided by the three reviewers.

**Reviewer #3:**

**N0. 1: Dear Authors I have read your manuscript with interest and found it worthy, thought it needs serious modifications, at least in my mind. You use past tense also in sentences where present tense sounds better. For example esophageal cancer was among the highest ranking...it was not it is still. There are nmore typos and on some points your text is a bit overcomplicated, hardly understandable. Please take care of these points. I attached the doc file with yellow markings where i have problems with the understanding or found questionable parts.**

Answer: We wholeheartedly concur with the reviewer's suggestions and think they are crucial. To take into account the reviewer's suggestions, we carefully revised the manuscript.

**N0. 2: Materials and methods should be described in a way, that everything would be reproducible. You forgot to write vendors and exact materials/tools you used. We do not know anything about the involved patients. Were they from TCGA? Or you just get the preliminary data and selection of the interesting genes from TCGA and later validated on your own cases? If latter, we do not know where these patients come from...you mentioned normal and cancer cases, but informed consent document is only about 151 patients. I think the found genes are not a top secret, so these should be mentioned in the abstract, too.**

Answer: We didn't make it obvious where the patients came from, which caused the reviewer a lot of difficulties. Data from the publicly accessible datasets TCGA and GTEx were used to evaluate the health of 653 normal controls and 151 patients with esophageal cancer. As a result, we have added this portion of the article's material.

**N0. 3: In discussion i would like to hear much more about the different prognostic factors in EAC and ESCC. And about targeted therapy. And about how your genes could help the therapy and decision on patients targeted therapy. Are these genes accessible somehow from biopsy or surgical material? By immuno or whatever? Your finding should need further validation and finding probable ways for incorporation into clinical practice.**

Answer: We appreciate the reviewers' input. As I said before, we revised the discussion part of the article and accepted the feedback from three reviewers. However, I must supplement the reviewer's comments with the following. Numerous prior research, including EAC and ESCC, have been done on the prognosis of esophageal cancer. As a result, rather than focusing on the many prognostic indicators for esophageal cancer, the discussion part of this research concentrates on the specifics of particular research on platelets, their genes, and the prognosis of esophageal cancer. My main goal is to draw attention to the connection between the prognosis of esophageal cancer and platelet-associated genes. Due to a lack of resources, we were unable to acquire anything about targeted therapy because our data came from the TCGA database. Some of these genes are obtained by surgical material removal, while others are obtained through biopsy. Our discussion section explains

that because our study is only a preliminary investigation, there has to be further validation before it can be used in clinical practice. This is also a limitation for us.

**N0. 4: Please check the tables and graphs very carefully, since BMI and follow up data are quite unbelievable, and all graphs should be self-explanatory.**

Answer: I appreciate the reviewer pointing up the mistake. Following our proofreading, we discovered that Table 1 did include inaccuracies. In accordance with the final statistics, we have rectified them.

**N0. 5: POINT-BY-POINT ANSWERS**

**1 Title. Does the title reflect the main subject/hypothesis of the manuscript? YES**

Answer: Thanks for the reviewer's approval.

**2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? NEEDS POLISHING**

Answer: We carefully revised the abstract in response to reviewer comments and enhanced language polishing using QuillBot (<https://quillbot.com/>).

**3 Key words. Do the key words reflect the focus of the manuscript? YES**

Answer: Thanks for the reviewer's approval.

**4 Background. Does the manuscript adequately describe the background, present status and significance of the study? NEEDS POLISHING AND COMPLETION**

Answer: We carefully revised the background, present status and significance of the study in response to the reviewer's remarks.

**5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? NEEDS COMPLETION**

Answer: We carefully revised the methods in response to the reviewer's remarks.

**6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? YES, BUT NEEDS COMPLETION HOW TO EXPLOIT THE RESULTS**

Answer: Thanks for the reviewer's approval. On the basis of the reviewer's suggestions, we have made further modifications and refinements.

**7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? NEEDS**

## **POLISHING AND COMPLETION**

Answer: We carefully revised the discussion in response to the reviewer's remarks.

### **8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? NEEDS POLISHING AND COMPLETION**

Answer: We appreciate the reviewers' input. Table 1 has certain inaccuracies, which we have examined for accuracy. Figure 3C was improperly used; it has been removed.

### **9 Biostatistics. Does the manuscript meet the requirements of biostatistics? YES**

Answer: Thanks for the reviewer's approval.

### **10 Units. Does the manuscript meet the requirements of use of SI units? YES**

Answer: Thanks for the reviewer's approval.

### **11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? NOT**

Answer: Thanks for the reviewer's comments. We make an effort to present the most recent, significant, and reliable sources in the introduction and discussion parts. There are no self-citations, omissions, incorrect or excessive citations of sources.

### **12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? NOT, NEEDS LANGUAGE POLISHING AND REWRITING IN A WAY TO BE BETTER UNDERSTANDABLE AND MORE COMPREHENSIVE**

Answer: Thanks for the reviewer's comments. The manuscript has through a rigorous editing process, and the language is now at a B level, if not A level.

### **13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting?**

Answer: The manuscript was prepared strictly according to the type of manuscript (Retrospective Cohort study).

### **14 Ethics statements. For all manuscripts involving human studies and/or animal**

**experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? QUESTIONABLE, NOT CLEAR INPUT DATA**

Answer: There were no human or animal blood or tissue samples used in the study; instead, the information came from open sources (TCGA datasets). As a result, there were no ethical concerns with this study.