OPEN PEER REVIEW

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Peer Review Report for "Evaluation of Epithelial-Mesenchymal Transition Genes Involved in Iranian Gastric Cancer Patients via Transcriptome Analysis"

Author(s): Shima Abed, Kaveh Baghaei, Parviz Pakzad, Mehrdad Hashemi, Mohammad Reza Zali

Review Timeline:

Submit Date: 4 Jun 2019
Revised Date: 25 Sep 2019
Accepted Date: 29 Sep 2019

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Associate Editor | **Revision** (0) 13 Aug 2019

Dear EIC,
In the current manuscript, authors have selected three genes based on the bioinformatics analysis to evaluate their expression in Iranian gastric cancer samples. Expression of the selected genes have been assessed previously in samples from other areas, so the study lacks novelty.
Other points are below:
1. Manuscript needs to be edited by a native English speaker as it has grammatical mistakes.
Examples: "Patients with gastric cancer mostly diagnosed in advanced stages…", "Gastric cancer classified…"
2. In the background section of the abstract, authors have stated that "a comprehensive study at the genomic level is needed", however, they have performed transcriptome analysis. Background should be related to the study design.
3. Number of assessed samples and controls should be mentioned in the abstract.
4. In the Introduction, authors have stated that "we have hypothesized that upregulation of

ECM components in gastric cancer, might induce EMT activation by inducing intracellular signaling pathways." However, their experimental method cannot verify this hypothesis. They have only compared expression levels of some genes between cases and controls. They did not perform any functional study too validate their hypothesis. So, I recommend author to restate their hypothesis.

5. The sample size of the study is too small to draw any conclusion. Can authors rationalize their sample size?

Thanks.

REFEREE: EIC | **Revision (0)** 13 Aug 2019

Dear Author,

Please revise your manuscript according to the comments and resubmit again.

Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Editor,

We are truly grateful to the reviewer's critical comments and thoughtful suggestions. Based on these comments and suggestions, we have made careful modifications on the original manuscript. We hope the revised manuscript will be acceptable for publication in the journal. Below you will find our point-by-point responses to the reviewer's comments. All changes are highlighted in manuscript.

Sincerely,

Associate Editor's Comments:

Associate Editor 1:
Dear Chief Editor
In the current manuscript, authors have selected three genes based on the bioinformatics analysis to evaluate their expression in Iranian gastric cancer samples. Expression of the selected genes have been assessed previously in samples from other areas, so the study lacks novelty.

Due to the personal medicine debate on gastric cancer and their high heterogeneity in different parts of the world, highlights the importance of a molecular regional study of the disease. Those genes were examined in Iranian patients as first time.

Other points are below:

Reviewer1;
1. Manuscript needs to be edited by a native English speaker as it has grammatical mistakes. Examples: "Patients with gastric cancer mostly diagnosed in advanced stages…", "Gastric cancer classified…"

Thanks for your comments and detail consideration, we checked manuscript again and all grammatical mistakes were improved. All changes are highlighted.

2. In the background section of the abstract, authors have stated that "a comprehensive study at the genomic level is needed", however, they have performed transcriptome analysis. Background should be related to the study design.

Precise point, it is considered in manuscript.

3. Number of assessed samples and controls should be mentioned in the abstract.

We added following sentence;

"THBS2, OSMR and CHI3L1 genes were selected for validation and verification in 25 confirmed adenocarcinoma gastric cancer patients and non-malignant normal tissues from Iranian population by real time PCR."

4. In the Introduction, authors have stated that "we have hypothesized that upregulation of ECM

components in gastric cancer, might induce EMT activation by inducing intracellular signaling pathways." However, their experimental method cannot verify this hypothesis. They have only compared expression levels of some genes between cases and controls. They did not perform any functional study too validate their hypothesis. So, I recommend author to restate their hypothesis.

Our hypothesis in the present study was to determine the most important genes involved in EMT processes by whole Transcriptome analysis and validate them in Iranian gastric cancer population. However, we restate to better convey our hypothesis. We replaced following sentence;

"Given the role of genes involved in EMT and subsequent malignancy in gastric cancer, we have carried out a bioinformatic analysis on raw data that were collected from RNA-seq published study."

5. The sample size of the study is too small to draw any conclusion. Can authors rationalize their sample size?

Given that the main purpose of this study was to identify the active genes in the EMT by analyzing the data and evaluation them in Iranian patients, 25 patients may indicate the role of those gene in gastric cancer. In a very prestigious study similar to our paper which published in Nature, 2017 (Evaluation of serum microRNA biomarkers for gastric cancer based on blood and tissue pools profiling, British Journal of Cancer volume117, pages266–273 (11 July 2017)), 20 patients with gastric cancer were involved for validation study. In the next phase of the current study, functional studies are needed to clarify the role of genes in the pathogenesis process.

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Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Associate Editor | **Revision** (1) 3 Sep 2019

Dear EIC,
The authors have addressed the mentioned points.
Thanks.

REFEREE: EIC | **Revision** (1) 4 Sep 2019

Dear Author
Please add the ethics committee approval of the study to the methods section in your manuscript.
Also, add the ORCID id of at least the first and corresponding authors in the authors section when submitting the revised manuscript. You can get an ORCID id from the ORCID website at https://orcid.org.
Thank you.

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear reviewers,

We are sorry for missing the figure number 1 in the text. Already it is highlighted in manuscript.

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: EIC | **Revision** (2) 29 Sep 2019

Dear Author,
This is my pleasure to announce you that your article has been accepted by the editorial committee after peer review in the International Journal of Cancer Management (IJCM). Hopefully, it will be published in future issues.
Thanks.