OPEN PEER REVIEW

## Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

## What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

## Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://brieflands.com/briefland/knowledgebase/category/tree.html#opr.html

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# Peer Review Report for "Non-invasive Prostate Cancer Detection by Measuring Expression Level of miR-21 and miR-214 in Urine"

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## Review Timeline:

Submit Date: 4 Oct 2020
Revised Date: 21 Nov 2020
Accepted Date: 23 Nov 2020

Revision (0)

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

**REFEREE**: Reviewer | **Revision** (0) 25 Oct 2020

Dear AE,
About the manuscript entitled; “Non invasive prostate cancer detection by measuring expression level of miR-21 and miR-214 in urine”, the subject of this article are good but the methods and statically analysis of the manuscript must be evaluated.
- In some part of manuscript general information was repeated. Please read manuscript again and deleted these sentences. Also, authors mentioned mir-21 and mir-214 is specific expressed in prostate cancer but there are some researches and reviews such as; The Promising Role of miR-21 as a Cancer Biomarker and Its Importance in RNA-Based Therapeutics. Mol Ther Nucleic Acids. 2020 Jun 5; 20: 409–420. That show mir-21 involved in many of cancer. Please explain clearly about selection this markers in introduction and discussion.
- For this study, the Patient consent and confidentiality form must be confirmed by Patients and mention in manuscript.
- In material and methods, please introduce and added references that used Trizol for extraction of mir (microRNA) .

- The statically analysis must be checked and added number of replication (repeat) for each sample (extraction and PCR).
- The statically analysis must be presented in figures 1 and 2.
- Figures legends must be explain clear exactly fig 1 and 2.
- The most of reference is old, please updated its.
- According to reference and discussion, there are some studies that reported same conclusion. Please explain innovation of your study. please explain and discuss about novelty of your works.
- The manuscript needs editing to bring its use of English up to standards.

Thanks

**REFEREE**: Associate Editor | **Revision** (0) 14 Nov 2020

Dear EIC,
The manuscript is studied, and there are some comments which should be addressed by the author. According to the comments, the document needs minor revision.
Kind regards,

**REFEREE**: EIC | **Revision** (0) 14 Nov 2020

Dear authors,
Please revise your manuscript according to the reviewer's and associate editor's comments. In addition, please define all abbreviations used in each table below that table. Also, in the keywords section, please remove "Biomarker", "miR-214", and "miR-21" from the list, as they are not considered MeSH terms. You should provide at least 3 keywords from MeSH main heading terms.
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,**

Many thanks for the efficient and valuable comments that you and the reviewers notated about the manuscript. We believe that it is very helpful to improve the impact of the manuscript. In the revised manuscript, we tried to apply all modifications according to each comment of the reviewers. The comments and answers are given below and highlighted in the revised manuscript.

Reviewer's Comments:

Reviewer 1:

Dear Authors,

About the manuscript entitled; "Noninvasive prostate cancer detection by measuring expression level of miR-21 and miR-214 in urine", the subject of this article are good but the methods and statically analysis of the manuscript must be evaluated.

- In some part of manuscript general information was repeated. Please read manuscript again and deleted these sentences. Also, authors mentioned mir-21 and mir-214 is specific expressed in prostate cancer but there are some researches and reviews such as; The Promising Role of miR-21 as a Cancer Biomarker and Its Importance in RNA-Based Therapeutics. Mol Ther Nucleic Acids. 2020 Jun 5; 20: 409–420. That show mir-21 involved in many of cancer. Please explain clearly about selection this markers in introduction and discussion.

- Reply: Duplicate sentences were removed. The reason for choosing these two microRNAs was explained in the text: " As mentioned, miR-21 inhibits expression of PTEN in prostate cancer and it can increase cancer cell proliferation and cause bone metastasis. miR-214 also controls various genes involved in prostate cancer, such as EZH2. Due to the study of these microRNAs in the serum and plasma of people with prostate cancer in previous studies, these microRNAs were selected and investigated in the urine samples. "

- For this study, the Patient consent and confidentiality form must be confirmed by Patients and mention in manuscript.

- Reply: All patients participated in this study with their Awareness and consent, and all patients were asked to fill out a consent form and their information was kept confidential. This issue was mentioned in the text.

- In material and methods, please introduce and added references that used Trizol for extraction of mir (microRNA).

- Reply: They were added in methods.

- The statically analysis must be checked and added number of replication (repeat) for each sample (extraction and PCR).

- Reply: The statically analysis was checked and extraction was performed once for each sample and qRT-PCR was repeated three times for each sample.

- The statically analysis must be presented in figures 1 and 2.

  - Reply: Figures 1 and 2 were edited and also the quality of the figures increased.

- Figures legends must be explain clear exactly fig 1 and 2.

  - Reply: Figures legends 1 and 2 were edited and explained clear.

- The most of reference is old, please updated its.

  - Reply: The references were updated.

- According to reference and discussion, there are some studies that reported same conclusion. Please explain innovation of your study. Please explain and discuss about novelty of your works.

  - Reply: In our study, these two microRNAs were investigated as a combined panel in urine of patients with prostate cancer in a larger group than other studies. Due to the low microRNA in the urine and the difficulty of studying it, less research has been done on urine. Other innovations of this research include study in two groups of metastatic and non-metastatic in patients with prostate cancer.

- The manuscript needs editing to bring its use of English up to standards.

  - Reply: The manuscript was edited and the errors were corrected.

Associate Editor's Comments:

Associate Editor 1:

Dear authors,

Thank you for submitting your manuscript to IJCM. There are some points that need consideration:

1. All abbreviations should be defined when they are used for the first time, both in the abstract and manuscript body, each one separately, such as RT-PCR.

- Reply: All abbreviations were defined for the first time, both in the abstract and manuscript body such as RT-PCR, PSA, DRE, BPH, ROC, AUC and ...

2. Please correct the following sentence: "MicroRNA can directly regulate oncogenes and tumor osteoporosis can play an oncogenic or tumor-assisted role, depending on the type of mRNA function they perform". What do you mean by "tumor osteoporosis"?!

- Reply: It is "tumor suppressor genes" and it was misspelled. This sentence was corrected to "MicroRNAs can directly regulate oncogenes and tumor suppressors genes, so they can play an oncogenic or tumor suppressor role depending on the function of their target mRNAs".

3. The manuscript need English editing, such as: "This microRNA can inhibit expression of tumors by PTEN gene suppressor" ?!

- Reply: The manuscript was grammatically edited and the spelling errors were corrected. Also, this sentence was corrected to " This microRNA can inhibit expression of PTEN (tumor suppressor gene) ".

4. "This microRNA is classified as an incomer"!! Do you mean "oncomir"?

- Reply: Yes, it is Oncomir and it was misspelled. This word was corrected in the text.

5. The authors have introduced mir-21 in the introduction section, but they have not done the same for mir-214.

- Reply: mir-214 was introduced in the background. "Another type of microRNA that plays a role in prostate cancer is miR-214. The miR-214 is one of the most important microRNAs plays a role in cancers especially prostate cancer, and the most important target mRNAs are *EZH2* and *CTNNB1* (14). It is located on chromosome 1".

6. In the methods section, you have mentioned that: "RNA with OD260/OD280 ratio between 1.8-2 was taken". This is actually the accepted ratio for DNA! The ideal pure RNA 260/280 ratio is 2- 2.2. Lower ratios denote contamination with either phenol or protein.

- Reply: The numbers in this sentence are wrong and this sentence was corrected to "RNA with OD260/OD280 ratio between 2-2.2 was taken".

EIC Decision:

Dear authors,

Please revise your manuscript according to the reviewer's and associate editor's comments. In addition, please define all abbreviations used in each table below that table. Also, in the keywords section, please remove "Biomarker", "miR-214", and "miR-21" from the list, as they are not considered MeSH terms. You should provide at least 3 keywords from MeSH main heading terms.

- Reply: All abbreviations used in each table were defined below the table. Also, "Biomarker", "miR-214", and "miR-21" were removed from the keywords section and the words "Prostate cancer", "MicroRNAs", and "Urine" were included as keywords.

**OPEN PEER REVIEW**

**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) 23 Nov 2020

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

**REFEREE**: EIC | **Revision** (1) 23 Nov 2020

Dear author,
This is my pleasure to announce to 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