OPEN PEER REVIEW

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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.

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https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

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Peer Review Report for "Evaluation of microRNA (411, 377, and 154) Expression in the Plasma and Placenta of Women with Preeclampsia"

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Review Timeline:

Submit Date:	16 Feb 2019
Revised Date:	1 May 2019
Accepted Date:	6 May 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: Reviewer | Revision (0)

18 Mar 2019

Dear AE,
The current manuscript is about the Evaluation of microRNA (411, 377, and 154) expression in the plasma and placenta of women with preeclampsia. The author studied the rate of three miRNA expressions in the placenta and plasma of normal and preeclamptic pregnancies. This subject is suitable for the journal of Gene, Cell, and Tissue But there are a few comments for the paper as below:
-The English language of the manuscript is not sufficient and there are still grammatical errors in the entire text. Please recheck it. Camma, dots, spacing, capital letters…….
- The style of the article and the fonts, figures, references are not in accordance with the journal of GCT. Please check the instruction for the author carefully.
- In the abstract, the conclusion is not clear and needs more details.
- The author examined the expression of three miRNAs (411, 377, and 154), why they selected these 3 elements? In this case, explain more in the introduction.
- In methods please explain completely in detail how to extract micro RNAs, synthesis of cDNA, design of primers, and PCR condition.
- In results, Explain the results for each item separately.
- The figures are not clear.

The discussion is very short and incomplete. In this section, compare the results with other articles.
Best regards.

REFEREE: Reviewer | **Revision** (0) 6 Apr 2019

Dear AE,
There are some comments which should be addressed by the author:
1. The text needs to be revised substantially in terms of grammar and writing style.
2-The criteria for the diagnosis of preeclampsia should be corrected.
3- At the sentence "In this study, we examined the expression of three miRNAs (411, 377, and 154) that have been associated with preeclampsia in pregnant women in various studies in serial blood samples and the placenta of normal pregnant women and pregnant women with preeclampsia" it seems that some references was omitted, furthermore, if previous studies showed the association of this microRNAs expression with preeclampsia, please explain the reasons for repeated of the Previous studies. in other word, it seems that your finding didn't have enough novelty.
4- Please define the company name and catalog number of used kits.
5- Please add the standard error of means of data to table 1.
6- Please add the reference of used primers to the text.
7- Please explain the method of real-time PCR results analysis.
8- The description of Fig. 1 is vague and unclear.
9- The discussion section is too short, for example why you focused on the role of environmental factors on microRNAs expression.
10- Please add the inclusion and exclusion of sample collection to the material an method section.
Thanks.

REFEREE: Reviewer | **Revision** (0) 7 Apr 2019

Dear AE,
There are some comments which should be addressed by the author:
1. Your Methods section is not well-organized, please revise.
2. What do you mean by this statement? "Standardization
was carried out using the real time method (Takara, SYBR® Premix Ex Taq ™)"
3. Please explain your reverse transcription method precisely.
Thanks.

REFEREE: Associate Editor | **Revision** (0) 7 Apr 2019

Dear EIC,
Based on the reviewers' comments and as I read, this manuscript needs major revisions. Please revised the manuscript and reply point to point to the reviewers' comments for re-evaluation.
Thanks.
Thanks.

REFEREE: EIC | **Revision (0)** 7 Apr 2019

Dear Author,

Based on the reviewers and AE comments this manuscript needs major revision.

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.

Reviewer 1:
hello dear sir/madam

1. your Methods section is not well-organized, please revise .

Thank you for your reminder, Materials and Methods were rewritten

2. what do you mean by this statement? "Standardization was carried out using the real time method (Takara, SYBR® Premix Ex Taq ™)"

Real-time PCR was performed by SYBR Premix Ex Taq (Takara, Japan) kit protocol

3. please explain your reverse transcription method precisely.

The total RNA from each sample was reverse transcribed into complementary DNA (cDNA) with gene-specific RT primers manually, primary reaction mixture of RT contained 3 µl RNA, 1.5 µl gene-specific RT primer(Table2) and 14 µl deionized water to a total volume of 20 µl, was heated at 70°C for 10 min, then secondary reaction mixture of RT contained 3µl RT buffer, 3µl deoxyribonucleoside triphosphates (dNTPs), 1 µl M-MLV reverse transcriptase, and 3 µl Deps water was added to first mix. RT reactions were performed for 15 min at 25°C, 15 min at 37°C, 60 min at 42°C, 10 min at 72°C and then held at 4°C

Reviewer 2:
Dear Editor in-chief
Current manuscript is about Evaluation of microRNA (411, 377, and 154) expression in the plasma and placenta of women with preeclampsia. The author studied about the rate of three miRNA expressions in the placenta and plasma of normal and preeclamptic pregnancies. This subject is suitable for journal of Gene, Cell and Tissue But there are a few comments for the paper as below:

Thank you for your reminder

1- The english language of the manuscript is not sufficient and there are still grammatical errors in the entire text. Please recheck it. Camma, dots, spacing, capital letters……..

It was done, I hope to be approved

2- The style of the article and the fonts, figures, refferenses are not in accordance with the journal of GCT. Please check the instruction for author carefully.

It was done

3- In abstract, the conclusion is not clear and needs more details.

It was done, I hope to be approved

4- the author examined the expression of three miRNAs (411, 377, and 154), why they selected these 3 element? In this case, explain more in introduction.

Because the three are located in a chromosome region and on the other hand, they are linked to pregnancy disorders.

-In methods please explain completely in details how to extract micro RNAs, synthesis of cDNA, design of primers, and PCR condition.

It was done, I hope to be approved

-in results, Explain the results for each item separately.

It was done, I hope to be approved

- The figures are not clear.

It was done

-The discussion is very short and incomplete. In this section, compare the results with other articles.
It was done, I hope to be approved

best regards

Thanks for your good advices

Reviewer 3:
1. The text needs to be revised substantially in terms of grammar and writing style.

Re-evaluated by the editor of a magazine

2- The criteria for the diagnosis of preeclampsia should be corrected.

Initial selection based on Doppler ultrasound was recommended by the prenatologist

Selection of probable candidates for preeclampsia in the 12th week (first trimester) was performed according to Doppler sonography for pregnant women. The health status of 70 pregnant women was evaluated until the end of pregnancy, 10 cases of women under study in the third trimester showed symptoms of preeclampsia(hypertension with a systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≤ 90 mmHg and proteinuria (≥1+))

3- at the sentence "In this study, we examined the expression of three miRNAs (411, 377, and 154) that have been associated with preeclampsia in pregnant women in various studies in serial blood samples and the placenta of normal pregnant women and pregnant women with preeclampsia" it seems that some references was omitted,

In the order of writing the reference was a mistake that was corrected

furthermore, if previous studies showed the association of this microRNAs expression with preeclampsia, please explain the reasons for repeated of the Previous studies. in other word, it seems that your finding didn't have enough novelty.

miR-411, miR-377, and miR-154 are located in a chromosomal area, and have been linked to pregnancy and some of the pregnancy disorders in past studies. Our goal was to search of a biomarker for early diagnosis of preeclampsia in pregnant women at risk. In this study, we examined the expression of three miRNAs in serial blood samples and the placenta of normal pregnant women and pregnant women with preeclampsia that have been associated with preeclampsia in various studies.

4- please define the company name and catalog number of used kits.

It was done

5- please add the standard error of means of data to table 1.

It was done

6- please add the reference of used primers to the text.

It was done

7- please explain the method of real-time PCR results analysis.

It was done

Real-time PCR was performed by SYBR Premix Ex Taq (Takara, Japan) kit protocol. The 11 µl PCR consists of 5.5 µl SYBR, 1 µl PCR forward primer, 1 µl PCR reverse primer, 2 µl cDNA template, and 1.5 µl D.W., all reactions were incubated at 95°C for 10 minutes, followed by 45 cycles of 95°C for 15 seconds, 60°C for 15 seconds, and 72°C for 30 seconds. All reactions were performed in duplicate with the use of the StepOnePlus Real-Time PCR System

8- The description of Fig. 1 is vague and unclear.

It was done, I hope to be approved

9- the discussion section is too short, for example why you focused on the role of environmental factors on microRNAs expression.

Oxidative stress seems to play a role in creating poor placentation in preeclamptic pregnancies, and it is effective on the expression of several miRNAs, including miR-377 and miR-210. Changes in environmental conditions may play a major role in creating this It should be noted that differences in the amount and manner of expression of placental miRNA in different methods have been reported. Sometimes, identified miRNAs in different studies have shown differential expression profile of miRNAs in human placentas that may be due to varying sensitivities of diagnostic methods, diversity in samples of different stages of pregnancy or individual differences. In addition to individual differences, it has been shown that factors such as race, body mass index (BMI), smoking status and mode of labor, affect the gene expression of a placenta, and can also change the expression of miRNA. Even the difference in the type of delivery, the presence and severity of pain may also lead to a difference in the expression of miRNAvariation

10- please add the inclusion and exclusion of sample collection to the material an method section.

It was done, I hope to be approved

Thanks for your good advices

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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: Reviewer | **Revision** (1) 5 May 2019

Dear AE,
The current manuscript is about the Evaluation of microRNA (411, 377, and 154) expression in the plasma and placenta of women with preeclampsia. The author describes the rate of three miRNA expressions in the placenta and plasma of healthy and preeclamptic pregnancies. They searched for a biomarker in the early diagnosis of preeclampsia in pregnant women at risk. In this study, the author examined the expression of three miRNAs in serial blood samples and the placenta of normal pregnant women and pregnant women with preeclampsia. It is an interesting subject and can provide a good idea to treat disease. This subject is suitable for the journal of Gene, Cell, and Tissue. The English language of the manuscript is sufficient. It was also well written and discussed. In addition, the authors have carried out reforms.
best regards.

REFEREE: Reviewer | **Revision** (1) 5 May 2019

Dear AE,
There are some comments which should be addressed by the author:
1- In table 1, please add the SEM after the corresponded values using the ± symbol.
2- Please, revise and correct some errors in the figures' legends, for example, the name of the microRNAs should be used in the correct format.
Thanks.

REFEREE: Reviewer | **Revision** (1) 5 May 2019

Dear AE,
All the comments are correctly placed in the manuscript.
best regards

REFEREE: Associate Editor | **Revision** (1) 6 May 2019

Dear EIC,
Based on the reviewers and as I read revisions were done well, minor revision in some figure must be done. However, in my opinion it can be accepted for publication in GCT.
Thanks.

REFEREE: EIC | **Revision (1)** 6 May 2019

Dear Author,
Based on the reviewers' and AE comments revisions were done well, minor revisions in some figures must be done. It can be accepted for publication in GCT.
Thanks.