

## **Evaluation of Th17 and Treg cytokines in patients with unexplained recurrent pregnancy loss (URPL)**

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1<sup>st</sup> Editorial decision

1-Nov-2021

Ref.: Ms. No. JCTRes-D-21-00073

Th17 and Treg cytokines in patients with unexplained recurrent pregnancy loss ( URPL): A comparison between local and systemic immune responses , new insights in URPL  
Journal of Clinical and Translational Research

Dear Prof Rafatpanah,

Reviewers have now commented on your paper. You will see that they are advising that you

revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Dec 01, 2021.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: The manuscript entitled: "Th17 and Treg cytokines in patients with unexplained recurrent pregnancy loss (URPL): A comparison between local and systemic immune responses, new insights in URPL" is interesting however has some flaws. The most prominent is English usage and punctuation marks across the manuscript. Suggestion to rename the "case group" for "URPL group". Instead of "deregulation" it will be better to use "dysregulation".

line 40 -maybe instead of "signature cytokine" - main cytokine. In methods there is not mentioned about sexual encounters in patients with URPL but it is discussed in methods: "Supernatants??? or cells?..were washed twice with phosphate buffered saline (PBS) (Sigma Aldrich) before their use."

There is no description about serum collection and hormones determination.

Il-10 only the gene expression in peripheral blood was measured. It will be interesting compare the results from endometrial and vaginal cells.

Table. 1: Clinical characteristics of subjects - please add the data from lab tests which are in- and exclusion criteria.

The description on the figures - it will be better refer groups as: "control group" and "URPL group", as well as "endometrium" instead of "endometr".

Please improve the discussion as well as conclusions (especially language usage).

Reviewer #2: Review: Excellent application, well-conducted with a rigorous and logical approach plan.

In the introduction section, I would like to mention the definition of Urpl in more detail.

In the method, the name of the kits used should be mentioned.

The paper is accepted with minor revise.

EDITOR: please ensure that the use of English language is in line with academic English as stipulated in our author guidelines.

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Authors' response

Date: November, 28, 2021

**The comparison of Th17 and Treg cytokines in local and systemic immune responses in patients with unexplained recurrent pregnancy loss (URPL): new insights in URPL**

Dear Editor

I would like to thank you of the valuable comments of reviewers which improve the quality of the manuscript. Please find the responses here, and in the revised manuscript in the yellow highlights and in Track change.

**Reviewers' Comments**

Reviewer #1: The manuscript entitled: "Th17 and Treg cytokines in patients with unexplained recurrent pregnancy loss (URPL): A comparison between local and systemic immune responses, new insights in URPL" is interesting however has some flaws. The most prominent is English usage and punctuation marks across the manuscript. Suggestion to rename the "case group" for "URPL group". Instead of "deregulation" it will be better to use "dysregulation".

**Respond**

*Thanks for this valuable comment, we replaced the terms as you advised us. We also checked the manuscript thoroughly and made grammatical corrections.*

-line 40 -maybe instead of "signature cytokine" - main cytokine. In methods there is not mentioned about in patients with URPL but it is discussed in methods: "Supernatants??? or cells?..were washed twice with phosphate buffered saline (PBS) (Sigma Aldrich) before their use."

**Respond**

*Thanks for this valuable comment, we replaced the terms and added sexual encounters in the result section.*

There is no description about serum collection and hormones determination.

**Respond**

*Thank you for this great comment, we added serum collection procedure section in the materials and methods section.*

-IL-10 only the gene expression in peripheral blood was measured. It will be interesting compare the results from endometrial and vaginal cells.

**Respond**

*Thanks for this valuable comment, because of limitation of our budget (considering Iran is under heavy sanctions) we were not able to measure IL-10 gene expression in endometrial and vaginal cells.*

-Table. 1: Clinical characteristics of subjects - please add the data from lab tests which are in- and exclusion criteria

**Respond**

*Thanks for this great comment, we added lab tests in the Table-3*

-Please improve the discussion as well as conclusions (especially language usage).

**Respond**

*Thanks for this useful comment. We edited thoroughly our manuscript. You can see the changes in the yellow highlights and in the Track change .*

Reviewer #2:

Excellent application, well-conducted with a rigorous and logical approach plan.

In the introduction section, I would like the mention the definition of Urpl in more detail.

**Respond**

*Thank you*

*In the method, the name of the kits used should be mentioned.*

**Respond**

*Thanks for this nice comment we added more details in the introduction section as you can see in the yellow highlights.*

Ref.: Ms. No. JCTRes-D-21-00073R1

Th17 and Treg cytokines in patients with unexplained recurrent pregnancy loss ( URPL): A comparison between local and systemic immune responses , new insights in URPL  
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Jan 12, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: Dear authors Thank you for the correction you have made.  
Please notice that the sentence is complicated: The reason of this idea can be bee stabilished by by previous the study which that indicated that in an established model mouse model of abortion, transvaginal TGF- $\beta$  promotes promoted a regulatory T-cellTreg cells response and and requitment of those cells to the vaginal and.This lead to decrease rate of abortion consequently decreasing the abortion rate [73].

Reviewer #2: The authors address all the issues.  
This paper is accepted in my side.

EDITOR:

Dear authors, thank you for submitting the revised version of your manuscript. After

deliberation with the reviewers the paper has been deemed publishable pending a few minor revisions.

The first minor revision is provided by reviewer 1. The second item that needs to be addressed is the language, which does not conform to our advertised and stipulated academic level English measure. Please proofread the manuscript thoroughly, preferably by engaging a native speaker or by contracting a third-party service. JCTR also has in house editors who could do a deep dive for a fee (in which case, please contact the editor at m.heger@jctres.com).

Thank you and looking forward to receiving a manuscript in pristine English with no punctuation and grammar/spelling errors.

Michal Heger  
Editor

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Authors' response

Date: Jan, 14, 2022

**The comparison of Th17 and Treg cytokines in local and systemic immune responses in patients with unexplained recurrent pregnancy loss (URPL): new insights in URPL**

Dear Editor

I would like to thank you for the valuable comments of reviewers which improve the quality of the manuscript. Please find the changes in the revised manuscript.

**Reviewers' Comments**

Reviewer #1: Dear authors Thank you for the correction you have made.

Please notice that the sentence is complicated: The reason of this idea can be established by previous the study which that indicated that in an established mouse model of abortion, transvaginal TGF- $\beta$  promotes a regulatory T-cell response and recruitment of those cells to the vaginal and. This led to decrease rate of abortion consequently decreasing the abortion rate [73].

**Respond**

*Thanks for this valuable comment, we revised the terms as you advised us.*

**Editor's comment**

Please proof read the manuscript thoroughly

**Respond**

*Thanks for this useful comment. We edited thoroughly our manuscript. You can see the changes in the revised manuscript.*

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3rd Editorial decision  
17-Jan-2022

Ref.: Ms. No. JCTRes-D-21-00073R2

Th17 and Treg cytokines in patients with unexplained recurrent pregnancy loss ( URPL): A comparison between local and systemic immune responses , new insights in URPL  
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Feb 16, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Dear authors,

Thank you for submitting the revision.

Firstly, I am always willing to be forthcoming to authors in terms of expedited processing for a special reason, but there are conditions. The main condition is that I am not prepared to do this at the expense of our journal.

With respect to your submission, the manuscript is replete with grammar/spelling errors that I requested you to avoid on 2 separate occasions: in the author guidelines and in my decision letter.

The consequence of ignoring my comments is that your manuscript is subjected to additional scrutiny. Accordingly, the following comments need to be implemented in addition to a linguistic overhaul to ACADEMIC LEVEL ENGLISH:

- 1) please shorten the title to cover the very essence of your study (or main conclusion)
- 2) please format the figures so that each panel is uniform in terms of graph dimensions and fonts used
- 3) the section on limitations needs to be expanded with [a] very small sample size and a statement that therefore [b] correlation cannot be viewed as causation and that therefore [c] studies in larger patient cohorts are needed to validate the observations and corollary conclusions.

Thank you and we are looking forward to your revised draft.

Michal Heger  
Editor

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Date: Feb, 16, 2022

**The comparison of Th17 and Treg cytokines in local and systemic immune responses in patients with unexplained recurrent pregnancy loss (URPL): new insights in URPL**

Dear Editor

I would like to thank you of the valuable comments of reviewers which improve the quality of the manuscript. Please find the changes in the revised manuscript. You can also find the track change of manuscript in the website as a supplementary file.

**Reviewers' Comments**

Accordingly, the following comments need to be implemented in addition to a linguistic overhaul to ACADEMIC LEVEL ENGLISH

**Respond**

Thanks for this useful comment. We edited thoroughly our manuscript. You can see the changes in the revised manuscript. We did our best, and we hope the revisions satisfy you.

- 1) please shorten the title to cover the very essence of your study (or main conclusion)



**Respond**

Thanks for this nice comment, we shorted the title.

2) please format the figures so that each panel is uniform in terms of graph dimensions and fonts used

**Respond**

Please find the changes in the revised manuscript.

3) the section on limitations needs to be expanded with [a] very small sample size and a statement that therefore [b] correlation cannot be viewed as causation and that therefore [c] studies in larger patient cohorts are needed to validate the observations and corollary conclusions.

**Respond**

Thanks for this valuable comment, we added the points in the revised manuscript.

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4<sup>th</sup> Editorial decision  
11-Mar-2022

Ref.: Ms. No. JCTRes-D-21-00073R3  
Evaluation of Th17 and Treg cytokines in patients with Unexplained Recurrent Pregnancy Loss (URPL)  
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Apr 10, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Dear authors,

I have eliminated most of the linguistic sloppiness from the manuscript. The revised version is appended to this email. Please continue in this draft and do not modify my revisions, otherwise I will be forced to reject your paper.

I need to you to complete the following:

- 1) Table 1: make sure all information is provided for each parameter for both groups. Also ensure the column headers are properly aligned. Report all quantitative data as mean  $\pm$  SD.
- 2) 18s should be written as 18S throughout the manuscript and figures (axis labels).
- 3) All figures on TGF-beta should be combined into 1 figure.
- 4) Figure 5: y-axis label should read: Frequency of sexual intercourse
- 5) The methods section lacks information on how data regarding sexual intercourse was gathered.

Please use track changes when making modifications so that I can assess the level of compliance.

There is additional documentation related to this decision letter. To access the file(s), please click the link below. You may also login to the system and click the 'View Attachments' link in the Action column.

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Date: April, 07, 2022

### **Evaluation of Th17 and Treg cytokines in patients with unexplained recurrent pregnancy loss (URPL)**

Dear Editor

I would like to thanks of the valuable comments of reviewers which improve the quality of the manuscript. Please find the responds here, and in the revised manuscript in in Track change format.

## Reviewers' Comments

- 1) Table 1: make sure all information is provided for each parameter for both groups. Also ensure the column headers are properly aligned. Report all quantitative data as mean +/- SD.

### Respond

*Thanks for this valuable comment, we addressed the issues in Table 1, you can find the changes in the revised manuscript.*

- 2) 18s should be written as 18S throughout the manuscript and figures (axis labels).

### Respond

- 1) *Thanks for this useful comment, we wrote 18s as 18S throughout the manuscript and figures.*

- 3) All figures on TGF-beta should be combined into 1 figure.

*Thanks for this useful comment. We combined Figure 2 and Figure 3*

- 3) Figure 5: y-axis label should read: Frequency of sexual intercourse

### Respond

Thanks we addressed this issue.

- 5) The methods section lacks information on how data regarding sexual intercourse was gathered.

Thanks for this great we use questionnaire for gathering this information. We added this notion in method section.

Ref.: Ms. No. JCTRes-D-21-00073R4

Evaluation of Th17 and Treg cytokines in patients with Unexplained Recurrent Pregnancy Loss (URPL)

Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Comments from the editors and reviewers: