Gene, Cell and Tissue
Volume 10 · Issue 1 · e115542

OPEN PEER REVIEW

Association Study of *TNF-α* -308 G/A (rs1800629) and -863 C/A (rs1800630) Polymorphisms with Systemic Lupus Erythematosus in the Iranian Lor Population

Zeynab Mashayekh, Mahsa Rafieian, Seyed Reza Kazeminezhad

SUBMITTED	REVISED	ACCEPTED	DOI
25 May 2021	6 Feb 2022	8 Feb 2022	10.5812/gct-115542

About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

More about open peer review: brieflands.com/knowledgebase/opr

Contents

1 **Original submission** Referee 1, Referee 2, Associate Editor, Editor-in-Chief 2
2 **Revision 1** Referee 2, Associate Editor, Editor-in-Chief 3
Authors' reply to reviewers 4
Reviewer and editor comments 6
3 **Revision 2** Referee 3, Associate Editor, Editor-in-Chief 7
Authors' reply to reviewers 8
Reviewer and editor comments 9
4 **Revision 3** Editor-in-Chief 10
Authors' reply to reviewers 11
Reviewer and editor comments 12
5 **Revision 4** 13
Authors' reply to reviewers 14
Reviewer and editor comments 15

1 Original submission

4 comments · 30 May 2021 – 7 Jun 2021

Referee 1 Reviewer

MAJOR REVISION 30 May 2021

The manuscript entitled “Association Study of the TNF-α -308G/A (rs1800629) and -863C/A (rs1800630) Polymorphisms with Systemic Lupus Erythematosus in Iranian Lur Population” evaluated the impact of TNF-α polymorphisms on the development of Lupus Erythematosus. The authors recruited 120 patients with SLE and 120 healthy controls and found some links between TNF-α polymorphisms and SLE. Although the manuscript has merit for publication, I found some issues that should be clarified and modified where necessary. My queries and recommendations are:
1- In the abstract, the full form of TNF should be used before using it as an abbreviation.
2- “Control group (n=120) was investigated among”: “were” should be used instead of “was.”
3- “among a sample population”: This would be better written as “among Lur population.”
4- There are 2 abstracts that differ from each other. In my opinion, Abstract 1 should be omitted.
5- Based on the information in Table 3, OR has been calculated incorrectly.
6- Thermal cycling is written incorrectly.
7- Grammatical errors are found throughout the manuscript and should be corrected. The authors should seek support from an English expert to improve the quality of the English.

Referee 2 Reviewer

MINOR REVISION 4 Jun 2021

Dear Authors
The paper appears comprehensive and the subject of the article is interesting. I have only a few concerns regarding the paper. Please check for grammatical mistakes, punctuation errors, and incorrectly used verbs or pronouns before submitting the paper. Overall, the paper is interesting and the topic is of interest to Gene, Cell and Tissue.
Take care of yourself during these days when the coronavirus is overshadowing everything.
Be successful and victorious.

Associate Editor

MAJOR REVISION 7 Jun 2021

Based on the reviewers' comments and my reading, this manuscript needs major revisions, and the comments need to be addressed point by point.

Editor-in-Chief

MAJOR REVISION 7 Jun 2021

Based on the reviewers' comments and my reading, major revisions to this manuscript and a point-by-point response to the comments are needed.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Reviewers' Comments and reply them:

Dear EIC

Thank you for giving us the opportunity to improve and resubmit our manuscript. The comments have been very thorough and useful in improving the manuscript. We strongly believe that the comments and suggestions have increased the scientific value of revised manuscript by many folds. We are submitting the corrected manuscript with the suggestion incorporated the manuscript. The manuscript has been revised as per the comments given by the reviewer. Changes to the manuscript are highlighted. We would like to thank the reviewer for the constructive and competent criticism.

Q 1: *Reviewer 1:*

The present article has major drawbacks in data analysis and study design, especially primer design in molecular analysis.

R 1: Data analysis and study design of this article are performed very carefully and we tested our primers in the first step.

Q 2: *Reviewer 2:*
The manuscript entitled “Association study of the TNF-a 308 G/A (rs1800629) and -863 C/A (rs1800630) polymorphisms with Systemic Lupus Erythematosus in Iranian Lur Population “evaluated the impact of TNF-a polymorphisms in the development of Lupus Erythematosus. The authors recruited 120 SLE and 120 healthy controls and found some links of TNF-a polymorphisms with SLE. Although the manuscript has merit for publication, I found some issues that should be clarified and modified where necessary. My queries and recommendation are:

1-In the abstract, the full form of TNF should be used before using as abbreviations.

2-Control group (n=120) was investigated among: Were should be used instead of was.

3-among a sample population: It is better written among Lur population.

4-there are 2 abstract that are different from others. In my opinion Abstract 1 should be omitted.

5-based on the information in Table 3, OR has been calculated incorrectly.

6-Thermal cycling written incorrectly.

7-Grammatical errors are found throughout the manuscript that should be corrected. Authors should take support from an English expert to improve the quality of English.

R 2: We modified all of 1, 2, 3, 4,6 and 7 recommendations and colored with green pencil. In case of 5 of your issues, this OR has been correct

Q3: *Reviewer 3*

Dear Authors

The paper appears comprehensive and the subject of the article is interesting. I have only a few concerns regarding the paper, please do check the grammatical mistakes, punctuation error and verb or pronoun if they add incorrectly before the submission of the paper. Overall the paper is interesting and the topic is of interest for Gene, Cell and Tissue.

R 3: we corrected mistakes of our manuscript and highlighted with light blue color.

Q 4: *Reviewer 4*

Dear editor manuscript is suitable for publication. I give some comments that authors should to answer and correct them.

1-In abstract part conclusions correct the lor and write capital word lor.

2-Background is weak and short please extends it.

3- You said several study in this part" several 70 studies have performed to analyze the association between rs1800630 at position -863 C/A 71 TNF-a promoter gene polymorphism and inflammatory disorders such as SLE. But the 72 different populations studied the results are shown the different "but you did not give reference.

4-explain this method simply" By using the salting-out method"

5-Inner primers write inner in lowercase.

R 4: We examined your comments then they are correct and highlighted with gray color.

2 Revision 1

3 comments · 10 Oct 2021 – 16 Oct 2021

Referee 2 Reviewer

ACCEPT 10 Oct 2021

Dear Authors,
The manuscript has been well revised.
best wishes

Associate Editor

MAJOR REVISION 16 Oct 2021

Based on the reviewer's comments and my reading of the manuscript, revisions have been made. However, this manuscript still needs major revision. Please revise it and reply to the comments.

Editor-in-Chief

MAJOR REVISION 16 Oct 2021

Based on the reviewer's comments and my reading, revisions were made. However, this manuscript still needs major revision. Please revise it and reply to the comments.

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Response to the reviewer 1:

Thank you for listening.

1- Check the length of PCR products.

- We used 2% and 2.5% agarose gel electrophoresis for detection of our products (TNF-a -308 & -863 polymorphisms, respectively) and had no problem recognizing the PCR products.

2- The sequence of one inner primer has a fundamental problem.

- All analyzes were performed by positive and negative control reactions.

3- Please explain that some internal primers can differentiate genotypes without any or one miss-match in their sequences?

- The polymorphism is located at the 3 prime inner primer sequences, and the long length of the primer sequence causes the primer to be specifically complementary to the sequence of interest.

4- In both polymorphisms, the authors reported the frequency of genotypes CC and GG as zero. How did they confirm the absence of these genotypes? While, they have a MAF of more than 0.1.

- There is a need to conduct studies at a larger level of the population. In our population AA allele have a MAF of more than 0.1.

5. In Table 2, the frequency of genotype C/A in patients is higher than in the control group, but the authors reported OR<1, explain the reason.

- Statistical analysis of the data was performed with SPSS® Statistics (Version 24) software. Odds ratio is calculated for AA & AC genotypes. The Table 2 has been reviewed.

Response to the reviewer 2:

Many thanks to you

Response to the reviewer 3:

Many thanks to you

3 Revision 2

3 comments · 27 Nov 2021 – 4 Dec 2021

Referee 3 Reviewer

MINOR REVISION 27 Nov 2021

According to the authors' answers (revision comments), they have designed the primers, have blasted the sequences, and the results have been confirmed with an attached agarose gel. The data for rs1800629 need to be recalculated (P value = 0.25, OR = 1.39, 95% CI 0.79 to 2.44).

Associate Editor

MINOR REVISION 4 Dec 2021

Dear Dr. Seyed Reza Kazeminezhad,

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 to each point raised when you submit the revised manuscript.

Yours sincerely

Bita Moudi, PhD
Associate Editor
Gene, Cell and Tissue

Reviewers' comments:
Reviewer 1.
According to the authors' answers (revision comments), they have designed the primers, have blasted the sequences, and the results have been confirmed with an attached agarose gel. The data for rs1800629 need to be recalculated (P value=0.25, OR=1.39, 95%CI 0.79 to 2.44).
Decision:
Minor revision

Editor-in-Chief

MAJOR REVISION 4 Dec 2021

Based on the reviewers' comments and my reading, this manuscript still needs major revisions, and the authors need to respond to the comments point by point.

4

Revision 3

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Dr. Bita Moudi,
Associate Editor
Gene, Cell and Tissue
Thank you for your email dated 12/04/2021 enclosing the reviewers' comments.
We have carefully reviewed the comments and have revised the manuscript accordingly.
Changes to the manuscript are shown in yellow.
Sincerely,

Reviewers' Comments:
Reviewer:
According to the authors answers (revision comments), they have designed the primers, have blasted the sequences and the results have been confirmed with an attached agarose gel. The data for rs1800629 needs to be recalculated (P value=0.25, OR=1.39, 95%CI 0.79 to 2.44)
Response: The data for rs1800629 was corrected and with yellow highlighted (please see table 2).

4 Revision 3

1 comment · 11 Jan 2022

Editor-in-Chief

MINOR REVISION 11 Jan 2022

Based on the reviewers' comments and my reading, this manuscript needs minor revision, and the authors need to reply to the comments point by point.

5

Revision 4

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Reviewers' Comments:
Reviewer 1:
In Table 2, re-check the percentage value for rs1800629.
R: This correction has been made and everything is now as it should be.

5 Revision 4

0 comments

No public comments in this round.