

This paper mainly discussed that TXNIP participates in regulating sterile inflammation including obesity and many microvascular diseases. Furthermore, some potential therapeutic drugs for targeting TXNIP expression were reviewed.

Overall, the authors focused on examining the contribution of TXNIP to expression and activation of NLRP3- inflammasome resulting in initiation or exacerbation of the disease state. This paper nicely showed the potential for TXNIP as a therapeutic target.

First, we would like to thank the reviewer for taking time to review our work and providing constructive comments. Please find answers below:

1: The logicity need to improve, focusing on how TXNIP function as the switch between oxidative stress and sterile inflammation according to the title.

The section "**1.2.TXNIP-NLRP3 Inflammasome Axis as a pivotal pathway for sterile inflammation**" has been expanded to elaborate on the postulated role of TXNIP as a common player in mediating cellular oxidative stress and also facilitating NLRP3 inflammasome activation (Page-7 of the revised file).

2: This manuscript mainly described sterile inflammation, authors should explain in detail the types of inflammation and define 'sterile inflammation'. The manuscript only focused on some types of sterile inflammation.

A new section and a new diagram were added "1.1 Sterile Inflammation as a physiological and pathological response". Further, additional details and new diagram that illustrates surface and cellular protein receptors involved in sterile inflammation.

3: The link between TXNIP expression and other miRNAs expression is not described except for miR-17-5p. Here needs a reasonable transition.

A new section about the role of microRNA in regulation of TXNIP is added. "**2.2 Role of microRNA and regulation of TXNIP expression.**" Examples of microRNAs other than miR-17-5p are now discussed (page9-10). Also, a new diagram (Fig.3) is now added to depict various ways of TXNIP regulation.

4: Although the paper described that obesity can lead to many microvascular diseases, it did not elaborate how these diseases are related to NLRP3 activation and the role of TXNIP. It will be nice to add detailed explanation.

A new section "**3.2 Direct role of TXNIP-NLRP3 Inflammasome activation in microvascular dysfunction**" is added that elaborated on the direct role of TXNIP-NLRP3 inflammasome in driving the inflammation and microvascular dysfunction.

5: There are many inconsistencies in spelling, such as IL-1b, miR17-5p and mir17-5p. The language in the manuscript also needs to polish.

The manuscript has been carefully revised to maintain consistency in symbols and overall language.

6 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

1 Scientific quality: The manuscript describes a review of the thioredoxin interacting protein as a key molecular switch between oxidative stress and sterile inflammation in cellular response.

(1) Classification: Grade B;

Thank you

(2) Summary of the Peer-Review Report: The authors focused on examining the contribution of TXNIP to expression and activation of NLRP3- inflammasome resulting in initiation or exacerbation of the disease state. This paper nicely showed the potential for TXNIP as a therapeutic target. The questions raised by the reviewers should be answered;

A point by point response is provided. In addition, the revised manuscript included 3 additional figures/diagrams, new sections and additional 15 references are included.

(3) Format: There are 4 tables; Additional 3 figures/diagrams are added.

(4) References: A total of 95 references are cited, including 40 references published in the last 3 years; The number of references is updated to 110 in revised manuscript.

(5) Self-cited references: There are 12 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations (i.e. those that are most closely related to the topic of the manuscript) and remove all other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated;

The self-cited references (12) are all closely related to the topic of the review article. The number of references in the revised manuscript is 110 and as such the ratio is very close to 10% and we hope that this will be acceptable.

(6) References recommendations:

The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

No concern for improper references.

2 Language evaluation: Classification: Grade B.

3 Academic norms and rules: No academic misconduct was found in the Bing search.

4 Supplementary comments: This is an invited manuscript. The study was supported by National Eye Institute.

5 Issues raised: (1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

6 Re-Review: Required.

7 Recommendation: Transferring to the World Journal of Biological Chemistry.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Diabetes, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

5 ABBREVIATIONS

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, and mAb, do not need to be defined and can be used directly.

A table of abbreviation is now provided.

The basic rules on abbreviations are provided here:

(1) Title: Abbreviations are not permitted. Please spell out any abbreviation in the title.

(2) Running title: Abbreviations are permitted. Also, please shorten the running title to no more than 6 words.

(3) Abstract: Abbreviations must be defined upon first appearance in the Abstract. Example 1: Hepatocellular carcinoma (HCC). Example 2: Helicobacter pylori (H. pylori).

(4) Key Words: Abbreviations must be defined upon first appearance in the Key Words.

(5) Core Tip: Abbreviations must be defined upon first appearance in the Core Tip. Example 1: Hepatocellular carcinoma (HCC). Example 2: Helicobacter pylori (H. pylori)

(6) Main Text: Abbreviations must be defined upon first appearance in the Main Text. Example 1: Hepatocellular carcinoma (HCC). Example 2: Helicobacter pylori (H. pylori)

(7) Article Highlights: Abbreviations must be defined upon first appearance in the Article Highlights. Example 1: Hepatocellular carcinoma (HCC).

Example 2: Helicobacter pylori (H. pylori)

(8) Figures: Abbreviations are not allowed in the Figure title. For the Figure Legend text, abbreviations are allowed but must be defined upon first appearance in the text. Example 1: A: Hepatocellular carcinoma (HCC) biopsy sample; B: HCC-adjacent tissue sample. For any abbreviation that appears in the Figure itself but is not included in the Figure Legend textual description, it will be defined (separated by semicolons) at the end of the figure legend.

Example 2: BMI: Body mass index; US: Ultrasound.

(9) Tables: Abbreviations are not allowed in the Table title. For the Table itself, please verify all abbreviations used in tables are defined (separated by semicolons) directly underneath the table. Example 1: BMI: Body mass index; US: Ultrasound.