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PEER-REVIEW REPORT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 72416

Title: Long noncoding RNA X-inactive specific transcript regulates NLR family pyrin domain containing 3/caspase-1-mediated pyroptosis in diabetic nephropathy

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05917063
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2021-10-15

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-15 09:19

Reviewer performed review: 2021-10-18 02:30

Review time: 2 Days and 17 Hours

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The present study aims to explore the function and molecular mechanism of the lncRNA Xist that has been reported to play an important role in diabetic nephropathy (DN). By using in vivo (DN mouse models established by streptozotocin treatment), and in vitro models (human renal tubular epithelial HK-2 cells exposed to high glucose), authors show that Xist is highly expressed and controls pyroptosis, a highly inflammatory form of lytic programmed cell death with formation of a large supramolecular complex termed the inflammasome. By different experimental approaches (including Xist silencing/knockdown, exploitation of miR-15b-5p inhibitor, TLR4 overexpression), Xist was shown able to bind miR-15b-5p and TLR4 was identified as a target of miR-15b-5p Globally, the mechanism of Xist in DN pyroptosis proposed by authors is quite well supported. For each part of the results, the authors got the confident data. But there are still some questions need to be clarified by the authors. 1. Some studies showed that the rat DN model can be established by one intravenous injection of streptozotocin (50mg/kg). What is the difference between these two methods? One injection is helpful to minimize the stress which may result in some unpredictable effects on the results. 2. As we all know, the rodents are used to eating at night. So, collecting the blood sample at late in the afternoon may be better. Did the authors try, and is there any difference of the results between these two time points? 3. The authors showed some predicted information about binding between miR-15b-5p and Xist, and miR-15b-5p and TLR4 based on the database. Because the present study is conducted on human kidney cell line HK-2 and the rat model, there are two different species, I have to raise the question that these bindings happen on human only or happen on both human and rat. 4.Which

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kind of miRNA inhibitor was used in the present study? The most widely used method for inhibiting microRNA (miRNA) function is by steric blocking, using an oligonucleotide that is perfectly complementary to the mature miRNA target. These inhibitors form a duplex with the miRNA guide strand and prevent the miRNA from binding to its intended target. The qPCR assay may not be suitable for detecting the efficiency of this kind of inhibitor. The supplementary data of target gene expression by Dual-Luciferase reporters assay is necessary. 5.In Figure 5 and Figure 7, could the authors explain the reason why these studies conduced on the background of Xist knockdown? Additionally, there is no control group.

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Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2021-10-15

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-15 11:28

Reviewer performed review: 2021-10-21 13:15

Review time: 6 Days and 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This research is interesting and meaningful, but it is not suitable for publication in its present form due to some drawbacks. 1. In abstract, the motivation, or/and the specific question behind the topic should be provided to let readers know why authors choose this topic and how important it is. 2. Authors should note that the full name of an abbreviation in the manuscript should be written when it first appears. The full name of "LDH" "i.p." should be used when it first appears in the abstract. 3. In the manuscript, the authors used "XIST" and "Xist" interchangeably. 4. There is a grammar mistake in "long non-coding RNA (lncRNAs)". 5. Could the author describe the raising condition of the rats? 6. The description of DN model establishment and treatment section is not clear and needs to be more detailed. Please check and correct them in this section. 7. Please unify the description format of antibody catalog number and company. I suggest that the format be unified as: catalog number + company name + company location. Reagents should also be described in this way. 8. Please add the source of the pentobarbital sodium and the DAPI. 9. Regarding the English language issue, this manuscript still needs to go through rigorous language editing.