Peer Review File
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Reviewer A:

1) There are some mistakes in page 20, the description of in the paragraph is not coincident with the Fig 5.

Reply 1: Thank you very much for pointing out this mistake. The relative description has been corrected in our new manuscript.

Changes in the text: Podocytes express proteins of mesenchymal cells, such as desmin, FSP-1 and collagen I, during the process of EMT in DN (n=3, 3/10). Thus, desmin, FSP-1, and collagen I protein expressions were detected by western blot, immunohistochemistry, and immunofluorescence in vitro. Our results showed that desmin, FSP-1, and collagen I protein expressions were significantly increased in DN mice and high glucose cultured podocyte (Figure 6 A-F). The desmin, FSP-1, and collagen I mRNA expressions were detected by RT-PCR, and the results showed that, as compared with the NC group, desmin, FSP-1, and collagen I mRNA expressions were also significantly increased in the DN and HG groups. More importantly, TSN significantly decreased desmin, FSP-1, and collagen I protein and mRNA expression in DN mice and high glucose cultured podocytes (Figure 6 G, H).
Page 22, line 401-413

Comment 2.

2) It will be better if the positive control drug can be added in vivo.

Reply 2: Thank you for comment on this important concern. The positive control drug (XST) has been added in our previous study. It has been demonstrated that TangShenNing (TSN) has the equal curative effect as valsartan on proteinuria and renal function in DN [1]. This study want to explore the molecular mechanism of TSN in DN. Herein, the positive control drug was not added in vivo in our current study.

[1] CUI Fangqiang，GAO Yanbin，WANG Yuefen，JIANG Xincan，ZHAO Wenjing. Effect of Tangshenning on podocyte apoptosis in KK-Ay mice. Shanghai Journal of Traditional Chinese Medicine, 2020, 54(04):92-96.

Comment 3.

3) The quantity of the 24h urinary protein should be given to affirm the DN model is successful in vivo.

Reply 3: Thank you for comment on this important concern. The quantity of the 24h urinary protein of DN model has been added in our new manuscript.
Changes in the text: When 24-h urinary protein $\geqslant$500ug, KK-Ay mice were considered DNmice.
Page 6, Line 128-129

Comment 4.

4) It will be better if the discussion section is more deeply.

Reply 4: Thank you for comment on this important concern.

The discussion section has been revised in our manuscript.

Changes in the text: The revised contents has been displayed in Page 28, line 486-490 and Page 29, line 504-512.

Reviewer 3.

Comment 3.

1) Tang-Shen-Ning has multiple roles. Doesn’t other mechanisms than Wnt/ß-catenin work?

Reply 1: Thank you for comment on this important concern. There is growing evidence that the activation of Wnt/ß-catenin pathway is involved in podocyte EMT. Podocyte EMT induced by Wnt/ß-catenin pathway plays a critical role in the progression of DN. Herein, the effect of TSN on podocyte EMT, Wnt/ß-catenin pathway, and DN was explored in our study. Tang-Shen-Ning (TSN), as a kind of TCM complex, may have multiple effect on podocyte EMT in DN. Future research is needed to explore other mechanism of TSN for treating DN.

2) The scale bars of Figure 2D, Figure 4C and Figure 5C should also be added.

Reply 2: Thank you for the important comment. The scale bars of Figure 2D, Figure 4C and Figure 5C has been added in our manuscript.
Changes in the text: Page 18, Figure 3; Page 21, Figure5; Page 23, Figure 6