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PEER-REVIEW REPORT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 72816

Title: Functional annotation and enrichment analysis of differentially expressed serum proteins in patients with type 2 diabetes after dapagliflozin

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05477765
Position: Peer Reviewer
Academic degree: PhD
Professional title: Assistant Professor, Senior Researcher
Reviewer's Country/Territory: Russia
Author's Country/Territory: China

Manuscript submission date: 2021-10-30

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-11-14 09:00

Reviewer performed review: 2021-11-19 12:07

Review time: 5 Days and 3 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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 manuscript of "Functional annotation and enrichment analysis of differentially expressed proteins in serum of patients with type 2 diabetes mellitus after dapagliflozin treatments" by Zhao YX et al. is devoted to liquid chromatography-mass spectrometry analysis of peptides obtained from of the blood serum of T2DM patients before and after treatment with the selective inhibitor of SGLT-2 dapagliflozin. The authors found that after dapagliflozin treatment, 18 proteins such as alpha II B integrin and myeloperoxidase (MPO) displayed down-regulated expression and PCX pyruvate carboxylase (PCX) had up-regulated expression in T2DM. The role of αⅡβ integrin, MPO, and PCX in the regulation of multiple pathways has been discussed in detail. Furthermore, the serum differential expressions of MPO, alpha II beta integrin, and PCX proteins were validated by ELISA, and their levels were found to be correlated with clinical indexes in patients with T2DM. The authors demonstrated that the related indexes of islet function, such as FBG, HbA1c, FCP, FINS and HOMA2-IR, decreased in dapagliflozin-treated patients. The work is very interesting, well written and detailed. The manuscript may be accepted for publication after minor revision. Comments: 1. It is known that pyruvate carboxylase is a mitochondrial protein, and integrins are transmembrane receptors located on the cell membranes. The sources of these proteins in the patients' serum need to be discussed. 2. The possible effect of dapagliflozin treatment on mitochondria needs to be discussed in more detail. Some studies showed that T2DM is associated with the development of mitochondrial dysfunction in vital tissues and organs (DOI: 10.3390/ijms21186559), and the treatment with dapagliflozin may restore the ultrastructure and functions of mitochondria in experimental T2DM

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(DOI: 10.1016/j.mito.2021.06.008). 2. It is necessary to provide the catalog numbers of the BioRad kits used for the determination of MPO, alpha II beta integrin, and PCX proteins by enzyme-linked immunosorbent assay.

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PEER-REVIEW REPORT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 72816

Title: Functional annotation and enrichment analysis of differentially expressed serum proteins in patients with type 2 diabetes after dapagliflozin

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03477174
Position: Peer Reviewer
Academic degree: MD
Professional title: Associate Professor
Reviewer's Country/Territory: Turkey
Author's Country/Territory: China

Manuscript submission date: 2021-10-30

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-11-20 05:10

Reviewer performed review: 2021-11-25 05:56

Review time: 5 Days

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 [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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

SPECIFIC COMMENTS TO AUTHORS

1. How was the number of subjects included in the study determined? Power test and sample size calculation should be done. 2. Baseline values of the control group and compare results with the study group should be given. 3. Patients aged 25 years and older were included in the study. Type 2 diabetes usually occurs in people aged 35 and over. Were other types of diabetes exclude in the patients? 4. Authors gave only exercise and diet to the control group. The mean HbA1c values of the patients included in the study were 8. Is this ethically correct behavior? 5. The number of patients and controls included in the study is less than 30. Therefore, nonparametric tests such as Wilcoxon, spearman, and Mann-Whitney u should be used. 6. Table 2 has no contribution to the study.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 72816

Title: Functional annotation and enrichment analysis of differentially expressed serum proteins in patients with type 2 diabetes after dapagliflozin

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05477765
Position: Peer Reviewer
Academic degree: PhD
Professional title: Assistant Professor, Senior Researcher
Reviewer's Country/Territory: Russia
Author's Country/Territory: China

Manuscript submission date: 2021-10-30

Reviewer chosen by: Han Zhang (Online Science Editor)

Reviewer accepted review: 2022-02-13 15:47

Reviewer performed review: 2022-02-13 16:07

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] 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
Peer-reviewer	Peer-Review: [ ] Anonymous [Y] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript "Functional annotation and enrichment analysis of differentially expressed serum proteins in patients with type 2 diabetes after dapagliflozin" by Yan-Xue Zhao, Sarul Borjigin, Zhao-Li Yan has been significantly improved. The authors have addressed all my concerns. The revised version of the manuscript may be accepted for publication.