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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 46296

Title: ¬Screening the RFX6-DNA binding domain for potential genetic variants in patients with type 2 diabetes

Reviewer's code: 02446609

Reviewer's country: United States

Science editor: Ying Dou

Date sent for review: 2019-02-10

Date reviewed: 2019-02-15

Review time: 4 Hours, 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	[ ] Accept (High priority)	Peer-Review:
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[Y] Accept (General priority)	[Y] Anonymous
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Minor revision	[ ] Onymous
[ ] Grade D: Fair	[ ] Grade D: Rejection	[ ] Major revision	Peer-reviewer's expertise on the topic of the manuscript:
[ ] Grade E: Do not publish		[ ] Rejection	[ ] Advanced
			[Y] General
			[ ] No expertise
			Conflicts-of-Interest:
			[ ] Yes
			[Y] No

SPECIFIC COMMENTS TO AUTHORS

This study by Mahmoud et al analysed structural genetic defects could be present in the DNA binding domain of RFX6 in T2D patients that could potentially inhibit its function in diabetes using PCR and DNA sequencing. The study was prompted by previous

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findings that genetic variants that increased the risk of T2D are predicted to disrupt mainly the binding of RFX6 to genomic DNA indicating that RFX6 binding to X-box promoter motifs could be disrupted in T2D. The authors conclude that there is no any significant genetic variant that could affect the function of DNA binding domain of RFX6. The results are important because they excluded genetic variations in RFX6 as player in T1D pathogenesis. I have few minor comments: 1) The authors should use T2D instead of only T2 in the abstract 2) There are few minor typo and grammatical errors that need to be fixed.

Response to reviewer #1:

1) In response to the reviewer request, the "T2" has been replaced by "T2D" (abstract, page 3 of the edited manuscript).

2) In response to the editor request, the language of the manuscript has been edited and proofread by an expert in English language and minor errors have been fixed and corrected now (see attached certificate of English language editing).

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 46296

Title: ¬Screening the RFX6-DNA binding domain for potential genetic variants in patients with type 2 diabetes

Reviewer's code: 03465354

Reviewer's country: United States

Science editor: Ying Dou

Date sent for review: 2019-02-10

Date reviewed: 2019-02-15

Review time: 6 Hours, 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [Y] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In the proposed manuscript entitled "Screening the RFX6-DNA binding domain for potential genetic variants in patients with type 2 diabetes" Mahmoud and co-authors aim to investigate the potential presence of genetic mutations in the DNA binding

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domain of RFX6 gene. The protein coded in this gene is previously known to play a key role in the differentiation of the pancreatic beta cells and insulin synthesis and secretion. The present study is based on data from total of 283 individuals (141 patients with type 2 diabetes mellitus and 142 healthy controls) recruited from Jordanian medical centers. Based on the results from this study, there is no significant genetic variant in the DNA-binding domain that could affect the function of RFX6 in type 2 diabetes mellitus patients. In my opinion as a peer reviewer, the work is well designed and the manuscript is logical and written in a clear way. My only concern is the fact that there is a statistically significant difference between the age and the gender between the control and the diabetic group of individuals (Table 1 and p. 7). The authors may want to discuss this difference.

Response to reviewer #2:

We do agree with the reviewer that there is a statistically significant difference between the age of control and the diabetic group (screening study of IVS 6+31 C>T variant), and we have previously referred to such difference in result section (page 7). However, there is NO statistical significant difference between the gender between the control and the diabetic (table 1, screening study of IVS 6+31 C>T variant). So as for the difference in age, we believe that such difference would not impact the accuracy of the result, firstly because the difference between average age (diabetic ~ 50; control ~ 57) is a slight difference, which unlikely to affect the result. Secondly, if we look at other statistic factors such as the median, age range and mode of ages, which give us a better picture about the age distribution, we found that both diabetic and controls have similar age distribution (data not shown).

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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 46296

Title: ¬Screening the RFX6-DNA binding domain for potential genetic variants in patients with type 2 diabetes

Reviewer's code: 03469767

Reviewer's country: Iran

Science editor: Ying Dou

Date sent for review: 2019-02-10

Date reviewed: 2019-02-17

Review time: 21 Hours, 6 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [Y] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [Y] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

Calculation for sample size? how the researcher defined the T2DM? separation of results from discussion? discussion need to be re-write. baseline characteristics of participants?

Response to reviewer #3:

Calculation for sample size?

The sample size can be calculated based on Cochran's formula:

$$N = PQZ^2 / \Delta^2$$

Where, N=sample size

Z=standard error (z=1.96 for 95% confidence interval),

P=estimated allele frequency (%), expressed in decimals,

Q=1-P; also expressed in decimals,

Δ =acceptable sample error 5%, expressed in decimals.

(James E. Bartlett et al,. Organizational Research: Determining Appropriate Sample Size in Survey Research. Information Technology, Learning, and Performance Journal, 2001, 1; 43-50).

The mutant allele frequency for IVS6+31 C>T in our study was ~ 5%, and According to Cochran equation the acceptable sample size ≥ 73. In this study n=141, which gives more reliable statistical results.

How the researcher defined the T2DM?

All diabetic patients enrolled in this study were diagnosed with T2DM by professional pathologists and recruited from Jordanian medical centers.

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Separation of results from discussion?

We agree with the reviewer that the discussion should be separated. The discussion section has been now separated from the results.

Discussion need to be re-written?

We think the discussion section is well written and prepared. It would be clearer if the reviewer specify his comment.

Baseline characteristics?

We believe that we have already included some main baseline characteristics (e.g. age, gender, FBS, HbA1c) in Table 1.

INITIAL REVIEW OF THE MANUSCRIPT

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