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E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes
ESPS manuscript NO: 17289
Title: Epigenetic profiles of pre-diabetes transitioning to type 2 diabetes and nephropathy
Reviewer's code: 00607647
Reviewer's country: Argentina
Science editor: Fang-Fang Ji
Date sent for review: 2015-02-27 17:15
Date reviewed: 2015-04-25 22:28

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

It is an interesting prospective study, analizyng DNA methylation profiling in 11 pre diabetic and 2 control individuals. In addition hypomethylation may be associated to difference genes in the nephropaty progression. A small number of participants may weak the important conclusions of this study. It is important to describe the general characteristics of the population in a table for better understanding

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Name of journal: World Journal of Diabetes
ESPS manuscript NO: 17289
Title: Epigenetic profiles of pre-diabetes transitioning to type 2 diabetes and nephropathy
Reviewer's code: 00607642
Reviewer's country: China
Science editor: Fang-Fang Ji
Date sent for review: 2015-02-27 17:15
Date reviewed: 2015-04-26 11:02

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
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[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Manuscript Number: wjd/20150227163837 Title: Epigenetic profiles of Pre-diabetes transitioning to Type 2 Diabetes and Nephropathy The investigators collected samples from 11 pre-DM non-Hispanic white male subjects when they were diagnosed with Pre-DM and repeated after transitioning to T2DM, and from two control subjects for reference. Genome-wide screening for DNA methylation was carried out by using Illumina Infinium 27K methylation array. The authors reported that 694 CpG sites were hypomethylated and 174 were hypermethylated in the DNA obtained at the time of transition to T2DM compared to the DNA obtained at Pre-DM. Sixteen genes were selected to evaluate the association between DNA methylation and the development of chronic kidney disease. Hypomethylation is seen in all sixteen of the candidate genes. The authors concluded that there are a large number of methylation changes in the progression of Pre-DM to T2DM and during the development of chronic kidney disease. I have concerns about data presentation. I wish the authors could focus on only one "end-point" topic in the manuscript. I suggest the author to delete the CKD parts. I will suggest the Journal to invite the authors to

resubmit their manuscript. Major suggestion: 1. This manuscript contains two end-points of data analysis: (1) transition from pre-DM to DM; (2) development of CKD. I will suggest the authors to delete all results and discussion about the "CKD" because the samples were collected before and after the development of DM, not CKD. Too many topics in the manuscript create confusion for the readers. The CKD parts are not supported by the longitudinal design of the study. 2. Generally, the manuscript is well written although it is out of focus in data presentation and in the Discussion.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes
ESPS manuscript NO: 17289
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Reviewer's code: 00646289
Reviewer's country: Turkey
Science editor: Fang-Fang Ji
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
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		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Manuscript Number: 17289 The authors examined DNA methylation statuses in genomes of prediabetic subjects, and in the genomes of the same patients when they later on developed T2DM along with diabetic nephropathy. The information provided on hypomethylated and hypermethylated sites related to genes involved in glucose and fructose metabolism, inflammation, oxidative and mitochondrial stress and fatty acid metabolism, and possibly in diabetic nephropathy are valuable. Yet the comparison of the hypo and hypermethylated sites in the prediabetic and diabetic stages seem to be more informative compared to the that made using the data related to the control subjects, as the number of the control subjects is only 2. The number of the patients in the experimental group is also obviously not optimal, as the authors also state themselves. This number may be supported by future studies. However, the number of control subjects is far from providing a statistically convenient evaluation, and should be increased for this study to be conveniently informative in such grounds. Although the hypomethylation detected in six genes in all the patients who also developed diabetic nephropathy may indeed be an early marker for the disease, the

status in patients with T2DM who did not develop diabetic nephropathy will be important along with a higher number of patients analyzed, to get an accurate result. However, considering the difficulties in patient availability and follow-up in such studies, the results related to the current 11 patients evaluated should be published, and this issue should be considered in future studies. The gender of the patients (all male) is probably a coincidence, but it may be good for the authors to state that the selection was random in terms of gender. The paper should be re-read thoroughly for a couple of minor letter/word/grammar errors.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes
ESPS manuscript NO: 17289
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
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		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

There are some points that the authors should provide further explanation before being published 1. As a human subject study, the subject number should be expanded. 11 subjects are not enough to give any implications. 2. The number of control subjects is two. In statistic rule, the control number should at least outnumber the study subjects by 2 folds for comparison. 3. The 11 patients enrolled in this study are males. Is there any specific purpose when selecting the study subjects? The authors should give a reasonable explanation. 4. The authors should provide more clinical implications after finished this study. (can be mentioned in the discussion section)