

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Diabetes

**ESPS manuscript NO:** 32099

**Title:** PCSK9 AND CARBOHYDRATE METABOLISM: A DOUBLE-EDGED SWORD

**Reviewer's code:** 02636605

**Reviewer's country:** 0

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2016-12-28 14:03

**Date reviewed:** 2017-01-09 09:09

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

### COMMENTS TO AUTHORS

In the editorial submitted to the journal, authors discuss the potential effect of PCSK9 inhibitors on glucose metabolism and risk of incident diabetes. The issue is relevant since clinical trials and experimental data from animal models have shown conflicting results of these drugs on the risk of DM. The text is clear and well-written. The figure is clear and self-explanatory. Among the reasons raised by the authors to explain the neutral diabetogenic effects of PCSK9 inhibitors observed in clinical trials, it would be worth to mention that the addition of this drugs to statins in the trials may partially mask effects on glucose metabolism if there are mechanisms of action shared between the two classes. Furthermore, I have only minor observations to be considered: Page 5, paragraph 1: The numeral 3 is being used. Consider spelling out the number. Page 6 last paragraph: I suggest adding to the text the registration number of each trial according to Clinicaltrials.gov

### RESPONSE

We added the suggested comment that the addition of these drugs to statins in the clinical trials



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may partially mask their effects on glucose metabolism if there are mechanisms of action shared between the two classes (bottom of page 6). We now use “three” instead of “3” (page 5, first paragraph). We added the registration number of each trial according to [Clinicaltrials.gov](http://Clinicaltrials.gov) (page 7).

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**ESPS manuscript NO:** 32099

**Title:** PCSK9 AND CARBOHYDRATE METABOLISM: A DOUBLE-EDGED SWORD

**Reviewer's code:** 02446585

**Reviewer's country:** Iraq

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2016-12-28 14:03

**Date reviewed:** 2017-01-22 20:55

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

### COMMENTS TO AUTHORS

The present review highlights a promising target with significant importance in treatment of DM and dyslipidemia. However, I suggest inclusion of a diagram the explain the regulatory effect of PCSK9 on LDL-c receptors and the outcome of its targeting with drugs.

### RESPONSE

We added a figure that explains the regulatory effect of PCSK9 on LDL-c receptors and the outcome of its targeting with drugs on serum LDL-c levels (Figure 1).



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## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Diabetes

**ESPS manuscript NO:** 32099

**Title:** PCSK9 AND CARBOHYDRATE METABOLISM: A DOUBLE-EDGED SWORD

**Reviewer's code:** 02946445

**Reviewer's country:** Turkey

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2016-12-28 14:03

**Date reviewed:** 2017-01-25 18:55

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

### COMMENTS TO AUTHORS

Thank you for this comprehensive and satisfactory "editorial" Good luck.

### RESPONSE

We thank the reviewer for his kind comments.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Diabetes

**ESPS manuscript NO:** 32099

**Title:** PCSK9 AND CARBOHYDRATE METABOLISM: A DOUBLE-EDGED SWORD

**Reviewer's code:** 02946508

**Reviewer's country:** Japan

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2016-12-28 14:03

**Date reviewed:** 2017-02-06 13:30

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input checked="" type="checkbox"/> High priority for publication
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### COMMENTS TO AUTHORS

Important review and proposal of mechanism for new class lipid lowering medicine on glucose metabolism. The authors pointed out the possibility of 'counterbalanced' effect of PCSK9 inhibition on glucose homeostasis, but there are other possibilities, such as no significant effects rather than dual effect on glucose metabolism when PCSK9 is inhibited. If authors make a table for summary of known animal data, known human data, speculations and/or future studies for the theme, readers can obtain unbiased, organized knowledge.

### RESPONSE

We added a table in which available genetic, experimental and clinical studies regarding the association of PCSK9 with carbohydrate metabolism are summarized (Table 1).