



PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 39507

Title: Coagonist of GLP-1 and glucagon receptors ameliorates kidney injury in murine models of obesity and diabetes mellitus

Reviewer’s code: 02624393

Reviewer’s country: Spain

Science editor: Fang-Fang Ji

Date sent for review: 2018-04-24

Date reviewed: 2018-05-02

Review time: 8 Days

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

SPECIFIC COMMENTS TO AUTHORS

This is an excellent manuscript describing the results of an experimental research in mice with regards to the treatment with a coagonist of GLP-1R. The treatment of diabetes mellitus with GLP-1R agonists has been introduced only some years ago , with



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excellent results. MAJOR CONCERN: In the abstract and in Material & Methods the authors note that the doses of the coagonist used were 150 ugr/kbw, but in the table 2 the doses are 300 ug/kbw. Please can you clarify this important methodological issue ?. MINOR CONCERNS: - The terms GLP-1 and GCGR mat be completely described the first time , before the introduction of the initials. -INTRODUCTION: 3rd file, please eliminate "the":...were closely associated and together ... - RESULTS: after the text of figure 1: ... "Feeding" high fat diet (not "feeing" fat diet). - I personally find very well selected the molecules described to study the oxidative stress and the inflammatory status. In the same way, the techniques used to describe the glomerular and tubulo-interstitial lessions are very well selected and the lessions very well described. DISCUSSION: But due to the relevant findings of this research you may add some comments on the limitations of the study, - i.e. 10 individuals in each group of research animals-. On the other hand, and taking into account the applicability of this research to the clinics, you should be able to add some comments on the possible translation of these findings to the daily practice, because these experimental results are in agreement with some recent studies, such as LEADER, SUSTAIN-6 or AWARD-7, among others.

INITIAL REVIEW OF THE MANUSCRIPT

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Name of journal: World Journal of Diabetes

Manuscript NO: 39507

Title: Coagonist of GLP-1 and glucagon receptors ameliorates kidney injury in murine models of obesity and diabetes mellitus

Reviewer’s code: 00058696

Reviewer’s country: United States

Science editor: Fang-Fang Ji

Date sent for review: 2018-04-24

Date reviewed: 2018-05-04

Review time: 9 Days

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		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I have carefully read this new review manuscript. This is a preclinical study using 3 separate murine models. My major questions are summarized below: 1) Abstract does not summarize the 3 murine models. 2) Introduction should propose a



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hypothesis and then list specific aims to study the hypothesis. 3) First sentence in Materials and Methods: the authors either need to provide either a reference for or validation studies for their contention that they are studying a coagonist. 4) The table in Materials and Methods provides “Primer sequences” but does not presently aid in summarizing why the authors chose specific products for RT-PCR. In describing the RT-PCR methods, please consider using either “Semi-quantitation of the mRNAs” or “Normalization of the mRNA levels was performed”. 5) In the Discussion, please consider adding a Cartoon that summarizes the proposed pathway. 6) In the Discussion, there is no description of limitations of these studies; for example, protein malnutrition can alter blood creatinine levels and body weight; RT-PCR gene expression studies may reflect only “accidental transcription” since protein expression has not been studied. Minor Issues: 1) The title is not fully accurate; please consider elimination of “diabetes-induced” and please consider after “kidney injury” adding “in murine models of obesity and diabetes mellitus”. 2) Abstract, Results: consider in sentence starting with “Lipogenic” adding “expression” after each of the two “gene”. 3) Abstract, Conclusion: Coagonist did not function by “restoring” obesity. 4) In Core tip, the second sentence is difficult to understand. Please consider after “alleviates” “biochemical and histopathological findings of nephropathy in HFSTZ and db/db mice”. 5) Core tip last sentence: do the authors mean “coagonist is effective”. The authors need to proof read their manuscript. There are other sentences missing verbs. The first sentence of the Introduction should probably read “Diabetes mellitus is often associated with”. 6) Last sentence of Introduction: do the authors mean “function in models of obesity and diabetes-induced”. 7) Materials and Methods: there is an incomplete address for Qiagen. In Materials and Methods consider specific labels for: Model 1. Renal dysfunction; Model 2. Streptozotocin-high-fat; Model 3. Genetic model of diabetes. Please provide a reference for the streptozotocin method. Then, “based



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of body weight”: which ranged from what to what ? 8) Obese mice were of what age? 9) Tissue sections were of what thickness? 10) Table in Results: Kidney weight is not in grams. Do the authors have any prior validation studies to demonstrate absence of edematous changes such as dry weight determination or result per mg protein? 11) Figure 1 in Results: this Figure needs to be able to stand alone and so the authors must be certain that all abbreviations are described in the Figure; p values should be shown in this Figure. 12) Table 3 in Results: this Table needs to be able to stand alone and so the authors must be certain that all abbreviations are described in the Table. 13) Figure 3 in Results needs to be able to stand alone and so it should be clear that mRNA levels have been normalized by secondary analysis of beta-actin expression. 14) Figures 4 in Results should be able to stand alone and so the authors must be certain that all abbreviations are described in the Figure. 15) Discussion paragraph 1: do the authors mean “in expression of lipogenic genes”. 16) Discussion paragraph 2, line 1: do the authors mean “Most obese individual never”. 17) In Discussion, the authors should consider noting that this preclinical study is an important initiation for translational research in this field of study.

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