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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 64251

Title: Tale of two kinases: Protein kinase A and Ca2+/calmodulin-dependent protein kinase II in pre-diabetic cardiomyopathy

Reviewer's code: 03649645
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Professor
Reviewer's Country/Territory: China
Author's Country/Territory: Mexico

Manuscript submission date: 2021-02-25
Reviewer chosen by: Ya-Juan Ma
Reviewer accepted review: 2021-05-29 06:24
Reviewer performed review: 2021-05-31 05:16
Review time: 1 Day and 22 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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 [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
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

MetS is a serious public health problem with increased risk for cardiovascular disease and DM2, leading to cardiac dysfunction in the form of prediabetic cardiomyopathy. In this paper, the author first introduced the role of PKA and CaMKII in cardiomyocytes, and discussed the establishment of predictive cardiopathy model in animals with different diets, then analyzed the reasons β AR/AC/Camp/PKA axis in predictive cartography and CaMKII as a novel target in predictive cartography. This review has clear logic, sufficient theory, and a certain degree of innovation, would allow for laying the foundation for rational design of targeted therapies to treat or prevent the development of pre-diabetic cardiomyopathy. There are some deficiencies in this view, there are several kinds of ADR in cardiomyocytes, however, it is not known how prediabetic cardiomyopathy alters β1-AR expression and signaling, it is recommended to find relevant literature to confirm this point of view. Furthermore, the references are well cited in the recent 3-5 years.

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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 64251

Title: Tale of two kinases: Protein kinase A and Ca2+/calmodulin-dependent protein kinase II in pre-diabetic cardiomyopathy

Reviewer's code: 02541960
Position: Editorial Board
Academic degree: MD, PhD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Mexico

Manuscript submission date: 2021-02-25

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2021-05-25 07:45

Reviewer performed review: 2021-06-02 13:00

Review time: 8 Days and 5 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
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

This review summarizes the current knowledge of the pathophysiological consequences of enhanced and sustained β-adrenergic response in prediabetes, focusing on cardiac dysfunction. This review also outlines recent information on the role of PKA and CaMKII in abnormal Ca2+ handling by cardiomyocytes. This article is well written and of clinical interest. Major comments 1 I would like to know the difference between prediabetic and overt diabetic cardiomyopathies, although I understand the primary focus of the review for prediabetic cardiomyopathy. 2 In the mechanism shown in Figure 1, the contribution of insulin resistance or hyperinsulinemia is unclear. Please add it into or explain in the text. 3 Is it possible to provide human study for the alterations in PKA or studies corresponding for such animal study? 4 The difference between presence ☑ and increase in the Table 1. For instance, presence of insulin resistance usually means the increase of insulin resistance. Minor comments It may be better to change the symbol of × (no change) to → and ☑(presence) to +.

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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 64251

Title: Tale of two kinases: Protein kinase A and Ca2+/calmodulin-dependent protein kinase II in pre-diabetic cardiomyopathy

Reviewer's code: 03701805
Position: Editorial Board
Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Mexico

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

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SPECIFIC COMMENTS TO AUTHORS

The interesting review by Gaitán-González et al summarized the current knowledge of the pathophysiological consequences of enhanced and sustained beta-adrenergic response in prediabetes, focusing on protein kinase A (PKA) and Ca2+/calmodulin-dependent protein kinase II (CamKII). The manuscript is well written, the figure and tables presented the most important message well. I have some suggestions: 1. Introduction: to emphasize the importance for recognizing the pathophysiological consequences of prediabetes, it is important to note that prediabetes, although still with controversy, observational studies and large sample meta-analyses had shown that prediabetes is associated with increased risk of cardiovascular disease and all-cause mortality in general population, as well as in those in baseline CVD (PMID: 27881363; PMID: 32669282) 2. Is prediabetic cardiomyopathy really exist or with clinical importance? I think it is true. Recently study also reported that prediabetes is associated with increased risk of heart failure. Such data further support the important term "prediabetic cardiomyopathy" proposed in this review. I suggest to cite these clinical findings (PMID: 33769672). 3. It should be note that the clinical definition of prediabetes including those with impaired fast blood glucose (IFG) and impaired glucose tolerance (IGT, 2 hour plasma glucose concentration 7.8-11.0 mmol/L during an oral glucose tolerance test). These two are reflecting different pathophysiological mechanisms in blood glucose regulation. However, not optimal animal models are suitable for distinguishing IFG or IGT models. 4. Keep consistent for the spelling of "pre-diabetic" with "prediabetic".