

Dear Editor,

Please find enclosed the revised manuscript ID 90731 titled "**Hypoxia-inducible factor-1 $\alpha$  in myocardial infarction**".

Authors: Ivana Škrlec and Sergey N. Kolomeychuk

Name of Journal: World Journal of Cardiology

Invited Manuscript NO: ID 05125057

Thank you very much for giving us the opportunity to revise our manuscript for possible publication in your distinguished journal. All Editorial and Reviewers' comments and recommendations have been addressed. In order to facilitate editing, all changes have been highlighted in yellow in the revised manuscript. Furthermore, all reviewers' comments have been inserted and also highlighted in yellow in our detailed response to reviewers, along with our change. We hope that this revision will satisfy the high standards of your distinguished journal. Please do not hesitate to contact me should any problems occur. We are looking forward to hearing from you at your earliest possible convenience.

The manuscript has been improved according to the suggestions of the Editorial Office and the reviewers:

### **Science editor comments**

**Thank you very much for the revision of our manuscript.**

Language evaluation: The English-language grammatical presentation needs to be improved to a certain extent.

**We provided the English Language Certificate issued by a professional English language editing company (Elsevier).**

Specific comments:

- (1) Please provide the filled conflict-of-interest disclosure form.

**We added the filled conflict-of-interest disclosure form.**

- (2) Please provide the Figures cited in the original manuscript in the form of PPT.

**The figure is an original image created by the authors for the manuscript. We have uploaded the original image as a PPT with all editable parts.**

(3) Please obtain permission for the use of picture(s).

The figure is an original image created by the authors for the manuscript, and permission is unnecessary.

(4) Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

We upload a copy of approved grants No. IP7-FDMZ-2023; No. 928-rp; No. FMEN 2022-0009.

### **Company editor-in-chief comments**

I have reviewed the Peer-Review Report, and full text of the manuscript, all of which have met the basic publishing requirements of the *World Journal of Cardiology*, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Done. The manuscript has been revised according to the peer-review reports and Editorial's comments. The changes have been highlighted in yellow in the revised manuscript.

### **Reviewer #1 comments**

The proposed editorial is an extremely interesting one, which brings to attention an important pathophysiological mechanism of myocardial infarction, which represents a significant future research direction due to its therapeutic and prognostic implications. The manuscript is very well designed, highlighting the importance of the topic and the need to include it in an editorial article. The scientific content is adequate, properly systematized. I congratulate the authors for their scientific approach.

We thank the reviewer for endorsing and supporting our manuscript.

## Reviewer #2 comments

The editorial manuscript described the roles of HIF1 $\alpha$  in hypoxic condition, such as myocardial infarction and the relationship between HIF1 and circadian rhythm. The manuscript is overall interesting and well written. I have a few minor comments.

We thank the reviewer for helpful comments, and we welcome his/her insightful suggestions that we have addressed.

Page 2, in the Abstract, PER2 needs full spell.

In the abstract, we wrote the full name of the PER2 abbreviation: period circadian regulator 2 (PER2).

Page 4, Line 6, by an oxygen-dependent process  $\rightarrow$  the meaning is not clear.

We rephrased the mentioned sentence to clarify it.

Under normoxia, HIF1 $\alpha$  is subject to oxygen-dependent hydroxylation.

Page 5, Line 8, cell type-specifically expressed  $\rightarrow$  the meaning is not clear.

The mentioned sentence was rephrased to provide clarity.

HIF1 $\alpha$  directly regulates over 1000 genes in the human genome during hypoxia, most of which are expressed in a specific cell type<sup>[9]</sup>. It is important to emphasize that this regulation is not an indirect, but a direct effect of HIF1 $\alpha$ .

Page 5, bottom line, after the cardiac-specific expression of HIF1 $\alpha$  increases during myocardial infarction  $\rightarrow$  The sentence is too complicated to understand.

The sentence was simplified by dividing it into two more straightforward sentences.

The signaling pathways mediated by HIF1 $\alpha$  and NF- $\kappa$ B show synergistic interaction to reduce cardiomyocyte apoptosis. Increased cardiac-specific *HIF1 $\alpha$*  expression during myocardial infarction leads to differential regulation of HO-1 and BNIP3 expression by HIF1 $\alpha$  and NF- $\kappa$ B<sup>[10]</sup>, demonstrating the crucial role of these signaling pathways in cardioprotection.

Page 7, middle, bHLH-PAS should be fully spelled.

We wrote the full name of the bHLH-PAS abbreviation: basic helix-loop-helix - Period-ARNT-Single minded (bHLH-PAS).

Thank you again for giving us the opportunity to revise our manuscript for possible publication in your distinguished journal.

Sincerely yours,

Assist. prof. Ivana Škrlec, PhD  
Faculty of dental medicine and health  
Crkvena 21 Osijek, Croatia  
Tel: +385912241437