

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Cardiology

**ESPS manuscript NO:** 20184

**Title:** Concepts of hypoxic NO signaling in remote ischemic preconditioning

**Reviewer's code:** 00607640

**Reviewer's country:** China

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2015-06-01 09:37

**Date reviewed:** 2015-07-06 10:04

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" 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 checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

The authors reviewed the effects of remote ischemic preconditioning (rIPC) applied by brief ischemic episodes to heart-distant organs tested in several clinical studies and discussed the possibly protective nitrite/NO signaling. It is suitable to the Journal and could be helpful in clinic study.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Cardiology

**ESPS manuscript NO:** 20184

**Title:** Concepts of hypoxic NO signaling in remote ischemic preconditioning

**Reviewer's code:** 00070389

**Reviewer's country:** United States

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2015-06-01 09:37

**Date reviewed:** 2015-07-07 04:34

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 checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input checked="" 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 checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

The paper should be revised in terms of English as well as the figure legend. For problems of English language, I have made revisions in the manuscript. For the figure legend, please emphasize that the two major sources of nitrite (and nitrate) include the endogenous L-arginine-NO pathway, and the diet, with conversion of nitrate from diet into nitrite by oral commensal bacteria. A. The classical L-arginine-NOS-NO signaling pathway. NO is produced in mammalian cells by an oxygen-dependent oxidation of a guanidine nitrogen of L-arginine. This multistep reaction is catalyzed by the heme-containing protein NOS, which also requires two flavin molecules and tetrahydrobiopterin as cofactors. In most endothelial cells, eNOS is regulated by calcium-dependent binding of calmodulin and by tyrosine phosphorylation. B. Nitrite reduction to NO is favored by decreasing physiological oxygen tensions and low pH, via nonenzymatic pathways or enzymatic pathways catalyzed by metal-containing enzymes.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Cardiology

**ESPS manuscript NO:** 20184

**Title:** Concepts of hypoxic NO signaling in remote ischemic preconditioning

**Reviewer's code:** 00227633

**Reviewer's country:** Portugal

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2015-06-01 09:37

**Date reviewed:** 2015-07-11 22:05

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 type="checkbox"/> [ Y] Grade B: Very good	<input type="checkbox"/> [ Y] 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"/> [ Y] No	<input type="checkbox"/> [ ] Minor revision
<input type="checkbox"/> [ ] Grade E: Poor		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"/> [ Y] No	

## COMMENTS TO AUTHORS

The manuscript is well written, very clear. I would eventually recommend the manuscript for publication after minor revision according to the suggestions described below. 1) Abstract more quantitative as possible, would favour the interest of the paper. 2) Figure is very good, and it should reflect as possible the main message. Eventually the last panel (or another figure describing the main targets of ROS on cell cardiac muscle would improve and go deeper to the message that the authors aimed to pursue. 3) Previous papers described the effects of RNS and particularly peroxynitrite on myosin, and also in calcium homeostasis and cytoskeletal structures as putative early effects of ROS, before targeting mitochondria. If there is ONOO association with ischemia/reperfusion insults and inflammation, it was also described a link between calcium concentration changes and cytoskeleton disruption. In our opinion some additional references should be include that would turn more sound and solid the present paper (please see for example: Tiago et al, Cell Calcium 49 (2011) 174-183;; Tiago et al, Biochemistry 2006, 45, 3794-3804; Tiago et al, BBRC 342 (2006) 44-49), namely for the understanding of the biochemical effects of ROS and RNS. 4) Ref 33 described the Kg of ATP per day. Several kg or it could be 700 kg! Kind regards