

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Biological Chemistry

ESPS manuscript NO: 21290

Title: Modulation of the matrix redox signaling by mitochondrial Ca²⁺

Reviewer's code: 00227420

Reviewer's country: Afghanistan

Science editor: Fang-Fang Ji

Date sent for review: 2015-07-10 15:22

Date reviewed: 2015-07-14 23:17

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"/> 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 checked="" 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 checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

In the present manuscript, Santo Domingo et al perform a nice review of what is known about the mechanisms that govern mitochondrial Ca²⁺ homeostasis and the role played by mitochondria in the regulation of cell redox equilibrium. The Authors also analyze the complex interplay between changes in mitochondrial Ca²⁺ levels and the regulation of mitochondrial matrix redox state. In my opinion, this is a well-written manuscript, characterized by a deep and thorough presentation of a rapidly moving field. The importance of the topic both in physiology and in pathology is highlighted, and all its aspects are dissected in a comprehensive and updated manner. Some minor typos: page 6, it is unclear the role of MICU1 oligomers (They should activate, not inhibit MCU1); page 7, depolarization of the inner mitochondrial (membrane) as a secondary consequence of LETM1..

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Biological Chemistry

ESPS manuscript NO: 21290

Title: Modulation of the matrix redox signaling by mitochondrial Ca²⁺

Reviewer's code: 00467115

Reviewer's country: Austria

Science editor: Fang-Fang Ji

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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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" 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 checked="" 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 checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The review by Santo-Domingo et al. gives a comprehensive overview on the molecules involved in mitochondrial calcium transport. The second part on redox signalling modulation is not well linked and should be revised. In general, this review would gain from some critical assessment of the literature and more linking of the topics discussed to the diseases mentioned only in the outlook. The abstract is somewhat self-contradictory: While first "the" protein involved in mitochondrial calcium transport is mentioned, later the (correct) referral is to several proteins. Bottom p. 3: NADPH is not – to my knowledge – generated by mitochondrial metabolism. p. 5: When discussing the composition of Unipex, all subunits should be referenced (not only MCU1). p. 6: The OMM still is a membrane and ions will not "freely" diffuse across it. Present understanding would suggest calcium enters via VDAC which is regulated and not constitutively open. p. 6: When discussing the results on EMRE knock-outs, the authors should offer an (hypothetical) explanation for the conflicting results. p. 7: revise sentence: "Depolarization of the inner mitochondrial..." p. 8: "ryanodine receptors" should not be capitalized. p. 9, line 4: Na⁺/Ca²⁺ exchanger. p. 9: "the inhibitor of mitochondrial Na/Ca" is slang. p. 12, line 16: membrane-permeant p. 13, line 8: our data establish



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p. 13, line 6 from bottom: β -cell (not beta-cells) p. 14, line 4: italicise "S" (3 times) p. 14: TCA cycle enzymes should not be capitalized, similarly carnitine on p. 15. The references have to be carefully checked; ie., second author ref. 17 should be Lillig HC.; second author ref. 18 is Schwarzlönder. Formatting in references also must be checked (e.g., refs .44, 45, 65, 67 and 69). Abbreviations should not be used without definition (e.g., MICU1) and a list of abbreviations should be included; once an abbreviation has been defined and introduced, it should be exclusively used (i.e., uncoupling protein 1, p. 14). All abbreviations used in a figure should be defined in the figure legend. Figure 2: histamine should not be capitalized in legend.