

## ESPS Peer-review Report

**Name of Journal:** World Journal of Biological Chemistry

**ESPS Manuscript NO:** 7174

**Title:** Thioredoxin and glutaredoxin-mediated redox regulation of ribonucleotide reductase

**Reviewer code:** 00227723

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-11-07 17:39

**Date reviewed:** 2013-11-17 11:26

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The authors provide a useful short review on redox regulation of ribonucleotide reductase. The review is informative for the reader who needs an introduction to this field. Better linking of the text to the figures would improve the final version. This is particularly true for Figure 2, in which many amino acids are indicated. The text does not describe the roles of these amino acids in detail. Addition of a few sentences to give this detail would help the readability of the review. The text is generally written clearly. There are a few required language corrections: Page 4: the the abstraction → the abstraction Page 5: the storage of radical → storage of the radical Page 6: Several evidences support → Several findings support Page 7 it has been also shown → it has also been shown Page 8: there exist a → there is a Page 8: In presence → In the presence Page 8: that the mammalian cells have have a → that mammalian cells have a Page 9: mothiol → monothiol Page 9: It suggests → This suggests Page 9: a study with mouse hepatocytes, suggested → a study in mouse hepatocytes suggested Page 10: in resting state → in resting state Page 10: the role of the thioredoxin system (or DTT) was suggested to facilitate the recognition of the network and allowing → the suggested role of the thioredoxin system (or DTT) was to facilitate recognition of the network and allow

## ESPS Peer-review Report

**Name of Journal:** World Journal of Biological Chemistry

**ESPS Manuscript NO:** 7174

**Title:** Thioredoxin and glutaredoxin-mediated redox regulation of ribonucleotide reductase

**Reviewer code:** 00289666

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-11-07 17:39

**Date reviewed:** 2013-11-19 00:35

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

In general, the authors have presented a nice, concise review of ribonucleotide reductase regulation, but there are a few issues that need to be addressed before the manuscript can be accepted for publication. First, the mechanism of RNR will be unfamiliar to the non-expert and thus a diagram of the mechanism should be the first figure in the review. Second, when discussing important residues in the R1 and R2 subunits (second paragraph of the "Classification and catalysis" section), no residue number are cited. This makes it difficult for the reader to reconcile the content of this paragraph with Figure 2. The authors should add these details to the text. In the section describing the role of Trx and Grx as electron donors, there are also a few problems. First, as a minor point, kcat should be lowercase, not uppercase. Second, the text refers to kcat/Km value, whereas the figure referenced show only the moles of product produced as a function of the different redox systems employed. Moreover, the trend cited in the text is not reflected in the figure. This leads to a very confusing presentation. Finally, the figure legends and figures need some work. In general, any reader should be able to look at the figures and figure legends and get a good sense of the paper. Figure 1 in the manuscript has only a minimal legend despite significant content. The authors should describe the ATP cone, which is circled, and its significance. There is a cofactor present shown in a CPK-like representation. This should be described. The color coding of the subunits themselves should be briefly noted. Finally, the magenta and reddish-brown subunits are too similar in color. Perhaps making one of them orange would be better. In figure 2, once again the legend is minimal. Important residues for RNR function are shown, but their roles are not described at all. At a minimum, the residues that form radicals should be highlighted in both the Figure and its legend. Moreover, these residues should be described in the text, along with citing the appropriate references describing their



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roles. The legend for figure 3 is fine, but the figure itself only shows redox on the left-hand subunit. The right hand subunit (I assume) undergoes the same process, but it is only partially depicted. If this was omitted for clarity, it should be noted in the legend.

## ESPS Peer-review Report

**Name of Journal:** World Journal of Biological Chemistry

**ESPS Manuscript NO:** 7174

**Title:** Thioredoxin and glutaredoxin-mediated redox regulation of ribonucleotide reductase

**Reviewer code:** 02445169

**Science editor:** Zhai, Huan-Huan

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	
<input checked="" type="checkbox"/> Grade D (Fair)	language polishing	BPG Search:	<input checked="" type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

This review article is written by experts in the field of thiol reductase. The prospect of targeting TR and GR to interfere with RNR catalysis also has great therapeutic value. However, a main concern of this review article is the lack of sufficient new information. In 2010, the same authors published a review article (Free Radical Biology & Medicine 49 (2010) 1617: 1628) that covered almost all key points of this submission, and the figures in this submission are either replicated or derived from the figures in the 2010 review article. The authors do mentioned some recent data, such as the 2012 Holmgren JBC paper about the ability of glutathion/glutaredoxin to reduce thioredoxin 1, but such new information is too little. The authors also included a paragraph discussing the role of thioredoxin system in the activity of class 3 RNR. However, such discoveries have been made more than 10 years ago. In summary, I feel that this submission in its current state does not contain sufficient new information to merit publication at World Journal of Biological Chemistry.