

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 19088

**Title:** Disruption of NAD<sup>+</sup> binding site in glyceraldehyde 3-phosphate dehydrogenase affects its intranuclear interactions

**Reviewer's code:** 02616129

**Reviewer's country:** Taiwan

**Science editor:** Xue-Mei Gong

**Date sent for review:** 2015-04-30 22:15

**Date reviewed:** 2015-07-24 16:30

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 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

In this study, Phadke et al. investigate the phosphorylated amino acid residues Y94, S98, T99 within the NAD<sup>+</sup> binding center of glyceraldehyde 3-phosphate dehydrogenase. Substitution of these amino acids with non-phosphorylated alanine residues did not abrogate intranuclear localization of GAPDH. Instead, such mutations altered the molecular dynamics parameters of intranuclear GAPDH probably by hindering its interactions with yet to be identified nuclear biomolecules. Molecular modeling experiments suggest an important structural feature -T99-E97 H-bond likely involved in stabilization of NAD<sup>+</sup> binding center. Overall, the work appears reasonable, well done and described. Only two minor points: 1. What happens will be the substitution of T99D? 2. Fig. 7 panel D. suggests to exhibit E97 position.

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 19088

**Title:** Disruption of NAD<sup>+</sup> binding site in glyceraldehyde 3-phosphate dehydrogenase affects its intranuclear interactions

**Reviewer's code:** 00505755

**Reviewer's country:** Japan

**Science editor:** Xue-Mei Gong

**Date sent for review:** 2015-04-30 22:15

**Date reviewed:** 2015-06-10 16:12

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 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input 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 type="checkbox"/> No	

## COMMENTS TO AUTHORS

General comments (1) The importance of the research and the significance of the research findings It is important research analyzing the effect of binding of GAPDH and NAD<sup>+</sup> and intranuclear interactions. (2) The novelty and innovative nature of the research It is novel in describing that GAPDH binding is associated with intranuclear interactions. (3) The quality of the manuscript's presentation and readability It seems okay. (4) The ethics-related aspects of the research N/A

Specific comments Title: It accurately reflects the major topic and contents of the study. Abstract: Please be consistent with amino acid abbreviations. Material and methods: In Transfection with pEGFP-GAPDH and FRAP experiments in page 8, in the equation  $D=0.88 \cdot w^2 / (4t_{1/2})$  for calculating diffusion coefficient, it seems to be  $\tau(\text{tau})_{1/2}$ , instead of  $t_{1/2}$ . Please check again. Results: The interpretation that GAPDH T99I mutant variant has affinity for glyceraldehyde 3-phosphate close to that of wild type enzyme may explain further, since the curve for T99I mutant in figure 4A has low saturation, even though the  $K_m$  of T99I is calculated as similar to that of wild type in Table 2. There might be some description about it. Discussion: The functions of GAPDH isoforms may be



## BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

<http://www.wjgnet.com>

---

described in detail in the first sentence in discussion. References: Please carefully check references again. Tables and figures: The legends for open or closed symbols may be added in figure 6.

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 19088

**Title:** Disruption of NAD<sup>+</sup> binding site in glyceraldehyde 3-phosphate dehydrogenase affects its intranuclear interactions

**Reviewer's code:** 02783515

**Reviewer's country:** United States

**Science editor:** Xue-Mei Gong

**Date sent for review:** 2015-04-30 22:15

**Date reviewed:** 2015-08-04 22:46

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

## COMMENTS TO AUTHORS

Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) is a multifunctional enzyme that is traditionally known for its role in the 6th step of glycolysis, yet studies have shown that this enzyme is implicated in other essential cellular processes beyond metabolism such as transcription activation, apoptosis, ER to Golgi vesicle shuttling, and axoplasmic transport. In the current manuscript, Phadke and colleagues examine the functional role of phosphorylated residues within the NAD<sup>+</sup> binding site of the protein. The authors convincingly show that the localization, the enzymatic properties and intranuclear interactions of GAPDH are affected by the phosphorylation status of these residues. Understanding the function of GAPDH, a protein involved in both metabolic and non-metabolic functions is significant and this study goes in this direction. Moreover, at least one variant, T99I, can be naturally present in melanotic melanoma cells. The experimental design is sound and therefore I have only minor concerns. 1) Part of these results appear to have been presented in preliminary form to some FASEB conference. The authors should mention this in the manuscript. 2) The manuscript lacks statistical analysis. 3) Figs. 5 and 6 scale bars are missing