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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 42991

Title: NKX6.3 protects against gastric mucosal atrophy by downregulating β-amyloid production

Reviewer's code: 00503623

Reviewer's country: United States

Science editor: Ruo-Yu Ma

Date sent for review: 2018-10-18

Date reviewed: 2018-10-22

Review time: 4 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[Y] Grade A: Excellent	[Y] Grade A: Priority publishing	[Y] Accept (High priority)	Peer-Review:
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] Accept (General priority)	[Y] Anonymous
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Minor revision	[ ] Onymous
[ ] Grade D: Fair	[ ] Grade D: Rejection	[ ] Major revision	Peer-reviewer's expertise on the topic of the manuscript:
[ ] Grade E: Do not publish		[ ] Rejection	[Y] Advanced
			[ ] General
			[ ] No expertise
			Conflicts-of-Interest:
			[ ] Yes
			[Y] No

SPECIFIC COMMENTS TO AUTHORS

This manuscript reports on the role of NKX6.3 transcription factor in the protection of gastric mucosa epithelial cells from atrophy by inhibiting AB peptide production and polymerization. By applying several advanced methods of analysis, the authors

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demonstrated Ab accumulation in the cytoplasm of HFE-145 cells and gastric mucosa with atrophy, and that NKX6.3 is a key regulator of gastric mucosal homeostasis by inhibiting the cell proliferation and apoptosis. Moreover, based on the obtained results the conclusion is that NKX6.3 suppresses gastric mucosal inflammation by modulation ApoE-induced NFkB and the expression of inflammatory IL-6 and IL-8 cytokines, and COX-2. Please correct English in the last sentence in the Summary.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

[ ] The same title

[ ] Duplicate publication

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[Y] No

BPG Search:

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[ ] Plagiarism

[Y] No

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 42991

Title: NKX6.3 protects against gastric mucosal atrophy by downregulating β-amyloid production

Reviewer's code: 00058340

Reviewer's country: United States

Science editor: Ruo-Yu Ma

Date sent for review: 2018-11-14

Date reviewed: 2018-11-21

Review time: 6 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	[ ] Accept (High priority)	Peer-Review:
[Y] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] Accept (General priority)	[Y] Anonymous
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[Y] Minor revision	[ ] Onymous
[ ] Grade D: Fair	[ ] Grade D: Rejection	[ ] Major revision	Peer-reviewer's expertise on the topic of the manuscript:
[ ] Grade E: Do not publish		[ ] Rejection	[Y] Advanced
			[ ] General
			[ ] No expertise
			Conflicts-of-Interest:
			[ ] Yes
			[Y] No

SPECIFIC COMMENTS TO AUTHORS

NKX6.3 protects against gastric mucosal atrophy by downregulating β-amyloid production Yoon JH et al. This is an interesting paper from experienced investigators postulating that NKX6.3 might play a critical role in the development of gastric mucosal

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atrophy by regulating Aβ production, and thus that Aβ can lead to gastric atrophy. The concept is novel, the studies were well designed and performed. Several issues, however, need to be clarified and elaborated upon. Comments: 1) The authors should elaborate more on amyloid peptides. Previous studies (see ref. 1 below) showed that in insulin producing islet cells of the pancreas the toxic activity is mediated by the fibrillar form of the peptide and that neurotoxicity is mediated by the βA fibrils, suggesting that a common mechanism of cell death may operate in many diseases associated with amyloid fibril formation. 2) They should provide more detailed information regarding βA. In Figure 3G description they said: "Immunofluorescence analysis showing expression of Aβ oligomer and Bace1 only in gastric mucosae with (W/) atrophy, but not in gastric mucosa without (W/O) atrophy." This is important Figure and should be of better quality and higher magnification allowing to determine whether expression of Aβ oligomer and/or fibrils is localized? - to cells epithelial cells only or also present in extracellular matrix. Congo red staining followed by illumination with polarized light would be very helpful. Do inflammatory cells produce βA? 3) Some studies (see ref. 2 below) showed that partial atrophy of the gastric mucosa in aging is not related to the inflammation. This should be discussed in the revised discussion. 4) The authors should provide a diagram representing their concept of gastric atrophy and the role of β-amyloid in this process. 1. Lorenzo A and Yankner BA. β -Amyloid neurotoxicity requires fibril formation and is inhibited by Congo red. Proc. Natl. Acad. Sci. USA Vol. 91, pp. 12243-12247, December 1994 2. A. Tarnawski et al. Aging gastropathy - novel mechanisms: hypoxia, upregulation of multifunctional phosphatase PTEN and proapoptotic factors. Gastroenterology 133:1938-47, 2007.

INITIAL REVIEW OF THE MANUSCRIPT

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[ ] The same title

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