

Answering the Reviewer and the Editor-in-Chief

Name of journal: World Journal of Gastroenterology

Manuscript NO: 48276

Title: How Does Helicobacter Pylori Cause Gastric Cancer Through Connexins:
An Opinion Review

We thank the reviewer and the editor-in-chief for their very thorough evaluation of our study and for their comments which have helped us to introduce important improvements in the new version.

In the following, we provide point-to-point answers to the comments of the reviewer and the editor-in-chief. The changes made in response to the recommendations of the Science Editor and the reviewer are marked in red in the new version of the manuscript. Hope to review patiently.

Reviewer's code: 00506472

SPECIFIC COMMENTS TO AUTHORS

It is a well written review regarding potential mechanisms of H Pylori induced gastric cancer through connexins. Please discuss in more details co-factors that may be involved in connexins induced mechanism of gastric carcinogenesis.

Answer:

Thank you for your comment. In response to your comment, we have searched and recruited some literature about co-factors that may be involved in connexins induced mechanism of gastric carcinogenesis. Furthermore, I think this theme should be further and deeper researches as I mentioned at the discussion of our article- "For all this, further and deeper studies between *H. pylori*-associated GC and Cxs are necessary." Thus, we have added some texts according to your comment:

For example:

"...it is ubiquitous in gastric tissues ^[39, 50, 61]. Cx43-dependent intercellular communication could spread cell death signals between neighboring cells through gap junctions^[44, 124, 125], using some candidate messengers such as Ca²⁺, cAMP, cGMP, and ATP^[124, 126]. *H. pylori* promoted the expression of GATA3..."

Dear Editor-in-Chief:

First, thank you for your comments and decision. I have seriously revised Our article as your comments and tips involving running title, ORCID number, telephone, fax, core tip and reference style mark with red color. Moreover, we will resubmit the supplement including language certificate, copyright license agreement, conflict-of-interest statement and audio core tip. Last, we have added "table 1" in order to better understand the distribution of Cxs in gastrointestinal and liver. Looking forward to your reply.

"...Cxs are expressed in a tissue-specific manner. **The expression of Cxs in the gastrointestinal tract and liver is presented in Table 1....**"

Table 1 Connexin expression in the gastrointestinal tract and liver

Tissue	Cell type	Species	References
Liver	Hepatocyte	Cx32/Cx26	[68]
	Kupffer cell	Cx43/Cx26	[69-71]
	Stellate cell	Cx43/Cx26	[70-72]

	Sinusoidal	Cx43/Cx32/Cx26	[70, 71, 73, 74]
	endothelial cell		
	Portal vein	Cx43/Cx40/Cx37	[75-77]
	endothelial cells		
	Hepatic artery	Cx43/Cx40/37	[75-77]
	endothelial cells		
	Cholangiocyte	Cx43/Cx32	[78, 79]
Stomach		Cx45/Cx43/Cx40/Cx37/Cx32/Cx26	[49-57, 80]
	Foveolar cell	Cx32	[81]
Small intestine			
	Musculus externa cell	Cx43/Cx40	[51]
	Myenteric Plexus cell	Cx45/Cx43/Cx40/Cx36	[51, 82, 83]
	Epithelial cell	Cx43/Cx37/Cx32	[51, 84, 85]
	Interstitial cell of Cajal	Cx43	[51, 86]
Colon			
	Musculus externa cell	Cx43/Cx40/Cx26	[51, 87]
	Myenteric plexus cell	Cx45/Cx43/Cx40/Cx36	[51, 83]

Epithelial cell	Cx43/Cx37/Cx32/Cx26	[85, 88-91]
Muscularis	Cx43	[51]
mucosal cell		
Interstitial cell	Cx43	[86]
of Cajal		
