



**Baishideng  
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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 53292

**Title:** Characterization and risk association of TLR2 polymorphisms and Helicobacter pylori with mRNA expression in gastric carcinogenesis.

**Reviewer's code:** 03260182

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Professor

**Reviewer's country:** Japan

**Author's country:** Brazil

**Reviewer chosen by:** Artificial Intelligence Technique

**Reviewer accepted review:** 2019-12-17 07:08

**Reviewer performed review:** 2019-12-25 07:42

**Review time:** 8 Days

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

## SPECIFIC COMMENTS TO AUTHORS



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Caroline de Matos Lourenço demonstrated that TLR polymorphisms are associated with gastric cancer in this manuscript. 1. I doubt statistical methods. For example, it is strange to compare three groups with three comparisons of two groups. 2. H. pylori infection is the most well-known risk of gastric cancer. TLR2 analysis should be performed after stratification for H. pylori infection.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

##### ***BPG Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 53292

**Title:** Characterization and risk association of TLR2 polymorphisms and Helicobacter pylori with mRNA expression in gastric carcinogenesis.

**Reviewer's code:** 00068458

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Doctor, Professor

**Reviewer's country:** South Korea

**Author's country:** Brazil

**Reviewer chosen by:** Jin-Zhou Tang

**Reviewer accepted review:** 2019-12-23 05:23

**Reviewer performed review:** 2019-12-27 01:51

**Review time:** 3 Days and 20 Hours

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

## SPECIFIC COMMENTS TO AUTHORS

The authors examined whether TLR2 19216T/C (rs3804099) and TLR2 -196 to -174 ins/del (rs111200466) polymorphisms contribute to gastric carcinogenesis in the Brazilian population. They found that two polymorphisms in toll-like receptor-2 (TLR2) are strongly associated with gastric cancer and *H. pylori* infection in the Brazilian population. In addition, TLR2 mRNA expression levels were upregulated in gastric cancer in the presence of the TLR2 -196 to -174 del variant allele or the wild-type TLR2 19216 T allele and in the presence of *H. pylori*. They conclude that The TLR2 -196 to -174 ins/del and TLR2 19216 T/C polymorphisms are strongly associated with GC. Although the findings are interesting, major revision is needed to better support this conclusion.

1. The case groups include 269 patients with chronic gastritis, 202 patients with gastric cancer and 381 patients without any gastric disease and *H. pylori* infection. 1) Total case number must be 852, not 854. 2) They included gastric disease-free control group (mean age = 51.26). The authors should explain how they confirmed histopathology of gastric lesion in this gastric disease-free group. In addition, because the mean age of this group is 51.26 and many people over age 50 have chronic gastritis, it is likely that gastric disease-free group has chronic gastritis. 2. In Fig. 3, carriers of the TLR2 -196 to -174 ins/del + del/del genotypes in gastric cancer patients had higher TLR2 mRNA expression levels than carriers of the ins/ins genotype. In addition, TLR2 19216 T/C+C/C variant carriers in gastric cancer patients showed reduced TLR2 expression levels with respect to TT wild-type genotype carriers. In chronic gastritis, there was no significant difference in TLR2 mRNA expression levels between TLR2 -196 to -174 ins/del + del/del genotypes and ins/ins genotype and between TLR2 19216 T/C+C/C and TT genotype. Thus, The authors need to explain why TLR2 expression in carriers of the TLR2 -196 to -174 ins/del + del/del genotypes and TLR2 19216 T/C+C/C variant significantly increased and reduced only in gastric cancer patients.



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## INITIAL REVIEW OF THE MANUSCRIPT

### *Google Search:*

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- ☐ No

### *BPG Search:*

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 53292

**Title:** Characterization and risk association of TLR2 polymorphisms and Helicobacter pylori with mRNA expression in gastric carcinogenesis.

**Reviewer's code:** 02533177

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Associate Research Scientist, Doctor

**Reviewer's country:** China

**Author's country:** Brazil

**Reviewer chosen by:** Jin-Zhou Tang

**Reviewer accepted review:** 2019-12-24 05:27

**Reviewer performed review:** 2019-12-30 04:53

**Review time:** 5 Days and 23 Hours

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

## SPECIFIC COMMENTS TO AUTHORS

The authors present that two polymorphisms in toll-like receptor-2 (TLR2 -196 to -174 ins/del and TLR2 19216 T/C) are strongly associated with gastric cancer and H. pylori infection in the Brazilian population; and that TLR2 mRNA expression levels are upregulated in gastric cancer tissues and modulated by both H. pylori infection and the presence of variant genotypes. That is interesting and significant for understanding the development of gastric cancer. However, there are some small issues in this manuscript.

1. In Figure 1, it is better to add the data of C group. 2. In "Subjects and Samples", the number of pylori- positive cases and pylori- negative cases in the CG group and GC group used to quantify TLR2 mRNA levels should be clear. 3. There are some spelling or grammatical errors throughout the manuscript. For e.g., in Table 2. TLR2 -196 to -174 ins/del(rs111200466)- Codominant - "in/ins" should be corrected. Please revise carefully.

## INITIAL REVIEW OF THE MANUSCRIPT

### *Google Search:*

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- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

### *BPG Search:*

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 53292

**Title:** Characterization and risk association of TLR2 polymorphisms and Helicobacter pylori with mRNA expression in gastric carcinogenesis.

**Reviewer's code:** 02941657

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Associate Professor

**Reviewer's country:** Thailand

**Author's country:** Brazil

**Reviewer chosen by:** Jin-Zhou Tang

**Reviewer accepted review:** 2019-12-23 07:11

**Reviewer performed review:** 2020-01-01 15:03

**Review time:** 8 Days and 8 Hours

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

## SPECIFIC COMMENTS TO AUTHORS



The author(s) studies genetic polymorphisms profile and genetic expression of specific gene, TLR2. There is a few studies and correlation of H. pylori prevalence. Brazilian H.pylori infection prevalence is quite low when compare to those in other Asian or other high prevalence countries. 1) Title: Characterization and risk association of TLR2 polymorphisms and Helicobacter pylori with mRNA expression in gastric carcinogenesis. comment: I think the author can arrange for better new heading to attract the audience by putting some words that specify the interesting result of this study. Example; is it dominantly found on which genotype? Do you find the strong correlation? 2) Abstract: In part of conclusion - I've not yet agree with the solution of gene modulate by H.pylori infection shown in mechanism in this study. Please, change wording or phrase. 3) Method: I understood that the author used relative quantitation method on gene expression results. I suggest the author to re-check statistic result with mean RQ that if it's non-normal distribution of population, you may use relative quantitation on log10 value to adjust the value distribution and then use median. 4) Results: - Please, add table: I wish I could see all demographic profile of population, but I can't see any table. Example; If the population of positive H.pylori distribution on each gene study group should be demonstrated that is clearer by writing in text. - Figure 1: Please, correct to clear comparative group. For the figure legend: I think the word "control" is not control group but standard samples for relative quantitation RT-PCR. - Figure 2: If you could arrange TLR-2 results in additional figure. Please, show 2 groups of positive H.pylori GC and CG VS negative H.pylori GC and CG. or A) GC - positive H.pylori VS negative H.pylori. B) CG - positive H.pylori VS negative H.pylori Figure legend should be clear to explain either. - Figure 3: showed the change between group of polymorphisms related expression. If the author can add figures of GC with each polymorphism profile with positive H.pylori/ negative H.pylori, it may explain related mechanism. 5) Biostatistical results: I wish I could see the error bar and stat label in the



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grafts of all figures between or among the comparative groups. 6) Conclusion: I've not yet agree with strong conclusion on H.pylori manipulation on TLR-2 gene expression and in each polymorphism types. Please, better show the detail of results for this correlation. This research is very interesting; however, more details of result should be demonstrated and revised.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

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