



**PEER-REVIEW REPORT**

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

**Manuscript NO:** 41572

**Title:** PIWI Y gene as a possible major player in gastric cancer

**Reviewer’s code:** 03317069

**Reviewer’s country:** Japan

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-08-14

**Date reviewed:** 2018-08-19

**Review time:** 5 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 checked="" 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**

In this study, the authors evaluated only one gastric cancer cell line to knockout PIWIL1 gene. It seems to be difficult to evaluate that PIWIL1 plays a crucial role in the signaling pathway of gastric cancer, regulating several genes involved in migration and invasion processes. The authors should evaluate the other gastric cancer cell lines except for



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AGP01 cell line. Moreover, the authors should evaluate the expression of PIWIL1 after knock down by RT-PCR or Western blot. Many genes were thought as candidates for the mechanisms used by PIWIL1 to promote carcinogenic effects related to migration and invasion. It is difficult to confirm which genes really related to migration and invasion from the results of literature.

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

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

- The same title
- Duplicate publication
- Plagiarism
- No

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

- The same title
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- Plagiarism
- No



**PEER-REVIEW REPORT**

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

**Manuscript NO:** 41572

**Title:** PIWI gene as a possible major player in gastric cancer

**Reviewer's code:** 03017551

**Reviewer's country:** Poland

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-08-14

**Date reviewed:** 2018-08-19

**Review time:** 5 Days

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 Grade E: Do not publish	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

**SPECIFIC COMMENTS TO AUTHORS**

First - this is a very important problem in the development and the treatment of gastric cancer. Second - this is a very interesting publication. Third - selection of references very good, interesting figures and tables,



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- No



**PEER-REVIEW REPORT**

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

**Manuscript NO:** 41572

**Title:** PIWI gene as a possible major player in gastric cancer

**Reviewer's code:** 00068458

**Reviewer's country:** South Korea

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-08-14

**Date reviewed:** 2018-08-22

**Review time:** 7 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 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 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 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**

This manuscript entitled "PIWIL1 gene as a possible major player in gastric cancer" studied functions of PIWIL1 in gastric carcinogenesis. The authors found that PIWIL1 gene knockout in AGP01 gastric cancer cell line by using CRISPR-Cas9 system induced a significant decrease in gastric cancer cell migration and invasion. In addition, they



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identified a total 35 genes encoding proteins involved in cellular invasion and migration. Of them, 9 genes are possibly related to the progression of gastric cancer. They concluded that PIWIL1 be a therapeutic target of gastric cancer. The idea is interesting. However, the pathophysiological relevance of the postulated evidences remains unclear. The reviewer has the following suggestions:

1. Previously, it has been reported that downregulation of PIWIL1 (hiwi) inhibited the growth of gastric cancer cells (Int J Cancer, 2006;118:1922-9) and the epithelial-mesenchymal transition (EMT) process of cervical cancer cells by regulating cadherin, vimentin and snail (Oncology Letters, 2018;16:3874-80). The authors should provide evidences showing that PIWIL1 regulates expression of EMT-related proteins in gastric cancer cells.
2. Gene expression analysis identified a total of 35 genes encoding proteins involved in migration and invasion of cancer cells and 9 of them are possibly related to the mechanisms used by PIWIL1 to promote carcinogenic effects.
  - 1) The authors should explain or provide evidences showing how PIWIL1 regulates expression of these genes.
  - 2) They selected 9 of 35 genes showing differential expression in the cell line before and after PIWIL knockout. The reason why they chose 9 genes is unclear.
  - 3) A total of 251 mRNA were found to be differentially expressed after PIWIL1 knockout in the cell line. Data presented up to this stage of the manuscript does not justify stating that PIWIL1 be a therapeutic target of the treatment of gastric cancer.
  - 4) DNA sequences or genetic status of 9 genes in the cell line before and after PIWIL1 knockout should be shown.
  - 5) The authors should also point out that PIWIL1 expression is closely associated with expression levels of 9 genes in gastric cancer tissues.
3. Mechanism for PIWIL1 overexpression in gastric cancer should be discussed.
4. Improve the resolution of Fig. 5.

## INITIAL REVIEW OF THE MANUSCRIPT

*Google Search:*



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- No

***BPG Search:***

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- Duplicate publication
- Plagiarism
- No



**PEER-REVIEW REPORT**

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

**Manuscript NO:** 41572

**Title:** PIWI Y gene as a possible major player in gastric cancer

**Reviewer's code:** 02687374

**Reviewer's country:** China

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-08-14

**Date reviewed:** 2018-08-23

**Review time:** 9 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:
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			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

This study established a permanent PIWIL1 gene knockout in AGP01 gastric cancer cell line using CRISPR-Cas9 system and analyzed phenotypic modifications, as well as gene expression alterations. The results showed that PIWIL1 plays a crucial role in the signaling pathway of gastric cancer, regulating several genes involved in migration and



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invasion processes; therefore, its use as a therapeutic target may generate promising results in the treatment of gastric cancer. The study is interesting. But it has some problems. 1. The English expression needs some modification. 2. Cell line AGP01 used in this experiment is established by author's group in 2009. It is recommended to add more classic gastric cancer cell lines to verify tumor invasion and migration. 3. This experiment lacks in vivo experiments to verify the role of the AGP01 in gastric cancer. 4. In Figure 4, it is recommended to compare the negative control group with the knockdown group. 5. The conclusions are overstated. For example, this study did not test the gastric cancer tissue samples, but found that the gene is associated with poor prognosis.

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