



## PEER-REVIEW REPORT

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

**Manuscript NO:** 39491

**Title:** FMN regulates RhoC/FAK pathway and actin assembly to promote cell invasion in colorectal carcinoma.

**Reviewer's code:** 03478911

**Reviewer's country:** South Korea

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2018-05-07

**Date reviewed:** 2018-05-14

**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 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

In this study, the authors investigated the invasion mechanism of colorectal cancer cell via formin-like 3 protein (FMNL3)-mediated enhancing RhoC/focal adhesion kinase (FAK) pathway. They argue that this pathway shows the effect of inducing metastasis of



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CRC cells. This study was well arranged and presented with good quality of results. However, this reviewer raises one major and some minor concerns. [Major concern] It has been reported that the induction of nuclear signaling by cleaved FAK increases the metastasis of colorectal cancer. Therefore, only the increase of FAK expression originating from various signals including FMNL3 and RhoC cannot explain the metastasis in CRC cells clearly. Therefore, the authors will have to provide an accurate analysis of the signaling cascades that can induce the metastasis of CRC cells from FMNL3 expression. [Minor concerns] \* Conclusion in Abstract: There is a lack of the description what phenomenon of FMNL3 has induced metastasis by remodeling of actin-based protrusions. \* Statistical analysis: In all results, statistical significance values of 'b' were presented as  $p < 0.01$ , which seems to require recalculation. The value inferred from the error bar is close to  $p < 0.001$ . \* Method for Figure 1: A detailed description of the method for inducing overexpression of FMNL3 in CRC cells is required. \* Figure 2: According to the Western blot results, FMNL3 was only down regulated. \* It should be described what shRNA1 and shRNA2 mean when using shRNA to down-regulate FMNL3. \* There are no discussion and review of the purpose and analysis of observing the expression between FMNL3 and F-actin. \* The explanation for the mechanism of metastasis by association of MMP-2 and MMP-9 expression through VEGF and/or RhoC should be discussed. \* There are many typos.

## INITIAL REVIEW OF THE MANUSCRIPT

### *Google Search:*

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- [ Y ] No



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***BPG Search:***

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

**Manuscript NO:** 39491

**Title:** FMN regulates RhoC/FAK pathway and actin assembly to promote cell invasion in colorectal carcinoma.

**Reviewer’s code:** 03551817

**Reviewer’s country:** China

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2018-05-07

**Date reviewed:** 2018-05-14

**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 checked="" type="checkbox"/> Grade B: Very good	<input checked="" 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**

In this manuscript, the authors clarified the underlying mechanism of formin-like 3 (FMNL3) promoting the invasion in colorectal carcinoma (CRC). That is, FMNL3 was initially activated by RhoC, followed by the activation of p-FAK and downstream of



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MAPK/ERK and PI3K/AKT signaling pathways, resulting in the increased expression of MMPs and VEGF. FMNL3 also accelerates the rearrangement of actin-based protrusions in a RhoC-dependent manner. These subsequently enhance the invasive capacity of CRC cells. It suggests a novel therapeutic regime for reducing cancer cell dissemination, blocking metastatic progression and prolonging life expectancy of patients with CRC. The article is comprehensive and worthy of our study. However, there is a minor problem in the article: 1. In the result of Western Blot, the form of presentation of MMP-2 and MMP-9 is inconsistent with other bands. Please confirm it.

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

**Manuscript NO:** 39491

**Title:** FMN regulates RhoC/FAK pathway and actin assembly to promote cell invasion in colorectal carcinoma.

**Reviewer's code:** 02569164

**Reviewer's country:** United Arab Emirates

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2018-05-07

**Date reviewed:** 2018-05-19

**Review time:** 12 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input checked="" type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input 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 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 checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
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### SPECIFIC COMMENTS TO AUTHORS

This is a well planned study with multiple experimental elements supporting the significant results. A reasonable conclusions were drawn from these experiments.



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- No