

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 42891

**Title:** Plasma and wound fluid levels of eight proangiogenic proteins are elevated after colorectal resection

**Reviewer's code:** 03478911

**Reviewer's country:** South Korea

**Science editor:** Jia-Ping Yan

**Date sent for review:** 2018-10-19

**Date reviewed:** 2018-11-01

**Review time:** 20 Hours, 12 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 type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" 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 authors performed screening for increasing angiogenic factors after resection of colorectal cancer. According to the results, they found the meaningful changes in the angiogenic-related factors after resection. However, many of the contents that were

described by the author is required a revision process. First: The authors must explain the mechanism of action of several angiogenic factors that listed in the theoretical background. And the purpose of the study that presented in the theoretical background is unclear. The authors need to describe the scientific and clinical implications to be gained by investigating the increase in angiogenic factors. Second: In the methodology, the factors such as the disease stage, sex, and age were not clearly distinguished. The various factors that presented by this reviewer are related to the outcome of treatment. Therefore, it can be an important parameter. The process of extracting proteins from tissues or blood is missing, therefore it needs further explanation. The method for calculating the error bar is missing. Third: In the POD1 results in Figures 1a, 1b, 2a, 2b, and 4b it seems that there are no statistical significance considering the error bars. Therefore, reanalyze is required. Discussion: It is better to describe the clinical implications, point by point, that can be gleaned from the author's findings, rather than theoretical explanations. Minor: It needs to under rigorous English correction.

## INITIAL REVIEW OF THE MANUSCRIPT

### *Google Search:*

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[ Y ] No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 42891

**Title:** Plasma and wound fluid levels of eight proangiogenic proteins are elevated after colorectal resection

**Reviewer's code:** 03721686

**Reviewer's country:** Romania

**Science editor:** Jia-Ping Yan

**Date sent for review:** 2018-11-27

**Date reviewed:** 2018-11-28

**Review time:** 10 Hours, 1 Day

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

The objective of this basic science study was to determine the 8 proangiogenic proteins that are significantly elevated over preoperative levels for 3 weeks after colorectal resection. Moreover, the authors demonstrated that the levels of these proteins in wound

fluid samples taken simultaneously from the pelvis and abdominal wall of CRC patients were significantly higher than the corresponding plasma levels at all time points. The idea of this study could be useful to highlight the importance of perioperative adjuvant/neo adjuvant therapy in malignant tumors and to further explore the process of normal wound healing vs. tumor angiogenesis. Besides the small number of patients included, the study has many limitations. Follow up of those patients would be of interest, especially the group with malignant pathology, to draw conclusions that are speculated in the text (e.g. Conclusion section- „These proangiogenic plasma changes may stimulate tumor angiogenesis during the first month after surgery in patients with residual tumor deposits post resection of the primary lesion”). Therefore, the conclusion may be revised to be concise. A table with histopathological details about tumors could be added (TNM staging, type of cancer, grading etc), as well as other causes, such as comorbidities, that could influence the results. Page 5, citation must be added- Recently, another mechanism has been proposed, namely the stimulation of angiogenesis in residual tumor deposits by persistent blood protein alterations. Page 6- the last phrase before Methods is unfinished-„ Of note, unlike previous plasma studies in which only 1 or 2 proteins were assessed on a given patient population, in this study, in all patients, plasma and wound levels of all 8 proteins were determined at each time point. In this study” Appropriate description should be added either in brackets for the first use of the abbreviation, or in legend – e.g. page 6-7- „This was an IRB approved prospective study.”; „Independent of this investigation, the authors have been investigating the use of subcutaneous wound drains to lower the incidence of superficial SSI's” etc.

## INITIAL REVIEW OF THE MANUSCRIPT

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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 42891

**Title:** Plasma and wound fluid levels of eight proangiogenic proteins are elevated after colorectal resection

**Reviewer's code:** 00183086

**Reviewer's country:** Greece

**Science editor:** Jia-Ping Yan

**Date sent for review:** 2018-11-27

**Date reviewed:** 2018-12-02

**Review time:** 21 Hours, 4 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	(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 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

This is a very interesting and well-written survey with regard to whether persistently elevated plasma levels of 8 proangiogenic proteins after colorectal resection are associated with greatly increased wound fluid levels of the same proteins. Nevertheless,



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in my opinion, revisions are required. 1. The Introduction section is too long. The number of paragraphs should be reduced and the aim of the study should be placed at the end of the section. Comparative evaluation of study's results should be referred in the Discussion. 2. In the Methods specific details of fluid collection could be omitted. On the other hand epidemiological data are missing. 3. In the Results information included in Tables should not be repeated in the text. 4. In the Discussion comparative analysis with other surveys is missing.

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

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- ☐ No



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 42891

**Title:** Plasma and wound fluid levels of eight proangiogenic proteins are elevated after colorectal resection

**Reviewer's code:** 03004570

**Reviewer's country:** Turkey

**Science editor:** Jia-Ping Yan

**Date sent for review:** 2018-11-27

**Date reviewed:** 2018-12-04

**Review time:** 1 Hour, 7 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	(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 checked="" 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 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 is a very well designed, prospective basic science study. There are some points to be corrected; Abstract contains two paragraphs of Results; this should be a repetition and must be corrected. The last sentence just before Methods must be corrected



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grammatically. When we look at the Results section in the manuscript, the number of APR is 10 (26%) in the cancer group, but it looks 9 (26%) in the Table 1. This must be corrected. Similarly, the number of Hartmann takedown with resection for benign group is 2 (6.5%) in the article, but 2 (7%) in the Table 1. The number of total colectomy/proctocolectomy is 3 (9.7) in the article, but 3 (10%) in the Table 1. These errors should be corrected. On the other hand, the figures are not visible clearly, it is not understood whether they are removed or not. I highly recommend those figures in the article. This trial gives very important and valuable information for clinicians especially future peri-operative anti-angiogenic treatments and worth publishing after minor corrections.

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

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

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- ☐ Plagiarism
- ☐ No

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

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- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 42891

**Title:** Plasma and wound fluid levels of eight proangiogenic proteins are elevated after colorectal resection

**Reviewer's code:** 03766000

**Reviewer's country:** China

**Science editor:** Jia-Ping Yan

**Date sent for review:** 2018-11-27

**Date reviewed:** 2018-12-05

**Review time:** 1 Hour, 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 type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
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		<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

In this study, authors investigated the changes of 8 proangiogenic proteins in serum and wound fluids of patients with colorectal resection, and found that all proteins increased obviously after colorectal resection, and the wound fluid protein levels were many fold

higher than corresponding blood levels. Major revision: 1 The sample size in this study is too small to obtain a solid conclusion. 2 I think there might not be a significant different in Figure 1a, 1b, 2a, 2b, 5a, 5b, 6a, 8a due to the big error bars. And authors did not provide SD or SE in tables. The data should be reanalyzed carefully. 3 Three-line table is the acceptable form worldwide. Please correct the tables. 4 There are many grammar errors in the manuscript. For example: Blood samples, collected in heparin coated vacutainers, were collected at the same time the WFL samples were obtained and then promptly processed via centrifugation at 450 G after which the plasma fraction was stored in labeled 500 ul cryo storage vials at -80°C until the time of analysis (Page 8).

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