

[2022-01-20]

[Editor]

World journal of Gastroenterology

Dear editor

I wish to re-submit the manuscript titled “Neutrophil extracellular traps participate in the development of gastric cancer associated thrombosis.” The manuscript number is: 72529.

We thank you and the reviewers for your thoughtful suggestions and insights. The manuscript has benefited from these insightful suggestions. I look forward to working with you and the reviewers to move this manuscript closer to publication in *World journal of Gastroenterology*.

The manuscript has been rechecked and the changes have been made in accordance with the reviewers’ and science editors’ suggestions. The responses to all comments have been prepared and are given below.

Thank you for your consideration. I look forward to hearing from you.

Best regards,

Xiaoming Zou (zou4930@163.com)

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Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Firstly, I would like to congratulate the authors for successfully conducting this very interesting study. It does provide great insight into the pathogenesis of VTE formation in gastric cancer patients. Unfortunately, there are certain limitations as below- 1. The manuscript is extremely long with multiple different experiments all clubbed together in one paper. It might be worthwhile to separate at least the in vitro and in vivo experiments. 2. Language and grammar polishing is required. 3. Please make sure all abbreviations are expanded.

1. The manuscript is extremely long with multiple different experiments all clubbed together in one paper. It might be worthwhile to separate at least the in vitro and in vivo experiments.

Response: Thank you for your excellent suggestion. I am very grateful to the reviewer for your affirmation of our work. We carefully analyzed the in vivo and in vitro experiments in the original manuscript. The original Figure 1 was mainly analyzed the NETs formation in clinical specimens of gastric cancer patients and original Figure 2, 4, 5 were the in vitro experiments about neutrophils, platelets and endothelial cells, and the Figure 6 was the in vivo experiment, only original Figure 3 included both in vivo and in vitro experiments.

In the revised manuscript, we have separated the in vitro experiments from in vivo experiments in according to your suggestion. The revised [Figure 3 \(flow cytometry analysis of activated platelets in peripheral blood of gastric cancer patients\)](#) was the in vivo experiment, and [revised Figure 4 \(isolated platelets were co-cultured with NETs\)](#) was the in vitro experiment.

2. Language and grammar polishing is required.

Response: We apologize for these careless linguistic mistakes. In the revised manuscript, we have modified these linguistic mistakes.

3. Please make sure all abbreviations are expanded.

Response: In the revised manuscript, we have ensured that all abbreviations were expanded.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: I read with pleasure and interest the manuscript entitled "Neutrophil extracellular traps participate in the development of gastric cancer associated thrombosis". It is based on the data of original research, well-written and scientifically consistent. The authors not only provided very detailed results, but also discussed possible implication of their findings for clinical practice. I suppose the manuscript brings new to the field and will be interesting to the readers. There are no major flaws. Only minimal correction (some typos) is required. Also, I would suggest to put the description of standard methods to the supplementaries, as well as some of the illustrations to keep up in accordance to the Journal's manuscript preparation requirements. **Congratulation to the authors for the great job done!**

Response: Thank you for your excellent suggestions. I am very grateful to the reviewer for your affirmation of our work. In the revised manuscript, we have modified these linguistic mistakes. Also, we have made necessary modifications to the description of standard methods and illustrations according to the requirements of the Journal's manuscript preparation.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The authors present an experimental study on the role of neutrophil extracellular traps in the development of cancer associated thrombosis. The manuscript describes a very well-designed experimental study, comparing NET levels in gastric cancer patients and healthy controls, and then evaluating the occurrence of thrombosis in a murine model inoculated with tumor cells. Writing in the english language needs to be extensively reviewed, as there are many grammar inconsistencies, such as: in page 3 line 28, "when compared to healthy individuals" would better convey the author's intention; page 4 line 1 "VTE is associated with a high mortality in GC patients"; page 4 line 15 "from pathogen-related damage"; page 6 line 5 "were obtained"; page 6 line 7 "The protocol";page 29 line 1 "found in lung vessels" or in "lung veins".

Response: Thank you for your excellent suggestions. I am very grateful to the reviewer for your affirmation of our work. In the revised manuscript, we have modified these grammar mistakes according to your suggestions.

Reviewer #4:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: this study is interesting and discusses an important issue for patients with cancer: 1- as regards table 1, please add a degree of freedom 2- as regards the figures, please add annotations, scale bar, type of stain or dye, magnifications, insets. 3- how you can use the results of this study for the favor of patients with gastric cancer.

1. as regards table 1, please add a degree of freedom.

Response: Thank you for your excellent suggestions. In the revised manuscript, we have added the degree of freedom (DF) in [Table 1 \(Characteristics, n=76, DF=4\)](#).

2. as regards the figures, please add annotations, scale bar, type of stain or dye, magnifications, insets

Response: Thank you for your suggestion. In the revised manuscript, we have added the annotations, scale bar, type of stain or dye, magnifications and insets in figures and figure legends.

3. how you can use the results of this study for the favor of patients with gastric cancer.

Response: In this study, we proved that NETs enhanced the blood hypercoagulable state of gastric cancer patients through the interaction with platelets and endothelial cells, and participated in the cancer-associated thrombosis. Future treatment strategies can consider the combination of traditional anticoagulant drugs and inhibit NETs drugs, so as to reduce the risk of cancer-associated thrombosis in patients with gastric cancer and improve the clinical treatment effect. From a clinical point of view, it is further envisaged whether DNase I, APC and sivelestat can be combined into new anticoagulants or thrombolytic drugs through nanotechnology or other new technologies, so as to change the current hypercoagulable state of gastric cancer patients and the treatment scheme of cancer-associated thrombosis.