



PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pharmacology and Therapeutics

Manuscript NO: 53452

Title: Shared changes in serum angiogenic factors across several distinct gastrointestinal vascular conditions.

Reviewer's code: 00054993

Position: Editorial Board

Academic degree: MD

Professional title: Emeritus Professor, Professor

Reviewer's Country/Territory: Austria

Author's Country/Territory: Ireland

Manuscript submission date: 2020-01-14

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-03-25 12:54

Reviewer performed review: 2020-03-26 17:25

Review time: 1 Day and 4 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

This pilot study in three small groups of patients with neovascularisation in the GI-Tract compares serum levels of angiogenic factors with those of a control group. The concept of the study is novel and so are the results and their interpretation by the authors. As discussed also by the authors, the main limitation are the small sample sizes of the 3 cohorts of patients and a significant difference of 17 years between the ages of patients and control subjects. Beyond that, several aspects need attention: The TITLE should point out the character of this study as a PILOT STUDY The ABSTRACT would gain in readability by omitting the detailed numbers for Ang-1 levels, similar to the description of Ang-2 levels. METHODS: Paragraph 1 describes exclusion criteria ..."known chronic liver disease _of_ non-liver-related portal hypertension". Most likely this should read ..._or_...? ..." 2 red tubes of blood were taken" ... What is the meaning of "red tubes" ? RESULTS: A current hemoglobin level was available in only 66% of subjects, which significantly lowers the validity of interpreting relevant results in the a priori small cohort of patients. Why could blood samples not be ascertained in about a third of patients? The Para "Serum levels of angiogenic factors" redundantly describes almost all numbers given in Table 1 anyway. Presentation either in the body of the manuscript or in the Table is suggested. The statement "Of interest, the median SBA Ang-1/2 ratio was similar to controls 21. Table 2" is not clear and should be checked and possibly rephrased. DISCUSSION: The statement in Para 2 "Ang-2 is known to be expressed ... etc." should be referenced. TABLE 1: As hemoglobin levels were ascertained in only 66% of subjects, the calculation and comparison of subjects with anemia of 13 patients (4+6+3) versus 1 Control is meaningless and should be omitted. FIG 1: The number on top of the second bar is reproduced incomplete (4678...) and this should be checked.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pharmacology and Therapeutics

Manuscript NO: 53452

Title: Shared changes in serum angiogenic factors across several distinct gastrointestinal vascular conditions.

Reviewer's code: 00049727

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Ireland

Manuscript submission date: 2020-01-14

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-03-25 03:20

Reviewer performed review: 2020-04-01 09:30

Review time: 7 Days and 6 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

The authors demonstrated that serum Ang1 levels were decreased and Ang2 were increased in patients having GI angiodysplasia. Although these findings seem to be interesting, there are some issues to be clarified.

1. The Ang/Tie receptor signaling cascades are involved in fundamental angiogenesis events. Both angiopoietins exerts angiogenesis-regulating effects via the angiopoietin tyrosine-kinase receptor (Tie-2). So I think the Tie2 level needs to be verified. Can you measure Tie-2 levels?
2. Figure 1 only shows the levels of Ang1 and Ang 2 in the disease group but not the levels in the control group. Comparisons with the control group may explain the expression levels of Ang1 and Ang 2 in several diseases more clearly.
3. In the Results section, the mean age (range) for the control group is shown as 49 years (range 20-74), but it is shown as 49 (range 24-60) in Table 1. The authors need to correct it.
4. In the Results section, the mean age (range) for 44 patients is shown as 60 years (range 18-93). Which group have 18 years old patient and which group have 93 years old patient, please explain it.
5. Abstract is redundant. Please revise it.
6. I am not sure if these angiopoietin changes are related to GI angiodysplasia. Are these produced at local angiodysplastic lesions and secreted into systemic circulation? To address this issue, I recommend to conduct immunostaining for ANG1/2 in surgically- or endoscopically-removed angiodysplastic lesions.
7. The weakest point for publication is too small sample size. Can you increase the number of samples?



PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pharmacology and Therapeutics

Manuscript NO: 53452

Title: Shared changes in serum angiogenic factors across several distinct gastrointestinal vascular conditions.

Reviewer's code: 02438768

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Ireland

Manuscript submission date: 2020-01-14

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-03-27 00:59

Reviewer performed review: 2020-04-05 02:20

Review time: 9 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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SPECIFIC COMMENTS TO AUTHORS

Comments for ESPS Manuscript NO 53452 This article is interesting. However, a small sample size makes it difficult to draw a convincing and reliable conclusion.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Manuscript NO: 53452

Title: Shared changes in serum angiogenic factors across several distinct gastrointestinal vascular conditions.

Reviewer's code: 00049727

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Ireland

Manuscript submission date: 2020-01-14

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2020-05-26 04:55

Reviewer performed review: 2020-05-26 05:00

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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SPECIFIC COMMENTS TO AUTHORS



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The authors responded properly but there are some limitations requiring further investigation.



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Author's Country/Territory: Ireland

Manuscript submission date: 2020-01-14

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2020-05-26 07:23

Reviewer performed review: 2020-05-26 09:18

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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The authors have responded adequately to my suggestions (Reviewer # 3); there are only minute typing discrepancies between their replies to the reviewers and the revised manuscript. Comments for ESPS Manuscript NO 53452, page 3: ..."2 red tubes of blood were taken"... is correctly explained as "serum separator tubes" in the reply, but the word "separator" is not included in the manuscript Last para of page 3: The reference to Table 2 (last line ...controls.Table 2) is not included in the manuscript