

PEER-REVIEW REPORT

Name of journal: *World Journal of Methodology*

Manuscript NO: 68551

Title: Interrogating the interplay of angiogenesis and immunity in metastatic colorectal cancer

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05562085

Position: Peer Reviewer

Academic degree: FRCS (Gen Surg)

Professional title: Academic Fellow

Reviewer's Country/Territory: Canada

Author's Country/Territory: Greece

Manuscript submission date: 2021-05-30

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-06-07 13:22

Reviewer performed review: 2021-06-07 14:07

Review time: 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 Grade E: Do not publish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
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
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SPECIFIC COMMENTS TO AUTHORS

Thank you for this review on a very important topic. The paper is well organized by topic. There are some minor improvements on the grammar and language that would make the paper easier to read, and it should be reviewed once more for those changes. Regarding the content-- On Page 6- you state "thus VEGF inhibits....the pathway" I beleve that is meant to read: "thus bevacizumab inhibits" - please verify this. Again, on page 6, you call results of VEGF research "contradictory". But go on to describe several consistencies, in that VEGF seems to be prognostic, but does not necessarily predict response to therapy. This should be clarified. In the section on MVD-- you use disease free survival and PFS as one outcome, but they are distinct and that should be clear. Overall it is a nice summary of the evidence.

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Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05601692

Position: Peer Reviewer

Academic degree: BPharm, MS

Professional title: Academic Research, Pharmacist, Research Scientist, Senior Scientist, Teaching Assistant

Reviewer's Country/Territory: United States

Author's Country/Territory: Greece

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Scientific quality	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Very good <input type="radio"/> Grade C: Good <input type="radio"/> Grade D: Fair <input type="radio"/> Grade E: Do not publish
Language quality	<input checked="" type="radio"/> Grade A: Priority publishing <input type="radio"/> Grade B: Minor language polishing <input type="radio"/> Grade C: A great deal of language polishing <input type="radio"/> Grade D: Rejection
Conclusion	<input type="radio"/> Accept (High priority) <input checked="" type="radio"/> Accept (General priority) <input type="radio"/> Minor revision <input type="radio"/> Major revision <input type="radio"/> Rejection

Re-review	<input type="checkbox"/> Yes <input checked="" 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

SPECIFIC COMMENTS TO AUTHORS

Summary: Colorectal cancer is one of the most common cancers affecting millions of people around the world. The effective treatment for the metastatic colon cancers includes the use of chemotherapeutic agents targeted against EGF-R, B-RAF and angiogenesis. In this review, the authors have reviewed the relevant literature and the recent advances on angiogenesis inhibitors focusing on Bevacizumab, a monoclonal antibody that targets VEGF-A. They also wrote a section on how the microvascular density increases during the progression of adenoma to adenocarcinoma through abnormalities in vasculature, and on how cancer cells enter the blood circulation enhancing tumor metastasis. The section on micro-RNAs which can serve as biomarkers is highly relevant and adds strength to the paper. Minor comments: My only suggestion is that the authors can briefly expand on the immune-check point inhibitors and their targets in the discussion section.