

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 59323

Title: Fork head box M1 regulates vascular endothelial growth factor-A expression to promote the angiogenesis and tumor cell growth of gallbladder cancer

Reviewer's code: 03724944

Position: Peer Reviewer

Academic degree: BSc

Professional title: Chief Technician

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2020-09-09

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2020-10-07 08:41

Reviewer performed review: 2020-10-16 11:09

Review time: 9 Days and 2 Hours

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 Grade E: Do not publish
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 checked="" 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

SPECIFIC COMMENTS TO AUTHORS

World Journal of Gastroenterology Manuscript N: 59323 Title: FoxM1 regulates VEGF-A expression to promote the angiogenesis and tumor cell growth of gallbladder cancer The authors demonstrate from in vitro and in vivo experiments that Fork head box M1 (FoxM1) is involved in the progression of gallbladder cancer (GBC) through the regulation of vascular endothelial growth factor A (VEGF-A) which plays an important role in neoangiogenesis processes. Furthermore, the authors show that FoxM1 is significantly more expressed in GBC than in paracarcinoma tissues, and this expression is positively related to that of VEGF-A in GBC tissues. This is an interesting study with a large number of important data and conclusions. However, I have some concerns regarding his presentation which I list below. -No information is given in the “materials and methods section” on patients whose tissues were used for FOXM1 expression (Figure 1A), qRT-PCR and western blot analysis ("4 paired GC clinical samples"), and comparison of FoxM1 and VEGF-A expression (48 gallbladder cancer tissues -Fig. 4A-D). -Methods used are described with little precision and lack important details. For example, it should be included the method for western blot, RT-PCR and IHC analysis, including the source and dilution of primary/secondary antibodies. - Figures have numerous panels representing data obtained with different methods. The legend of each figure should be more informative, indicating the corresponding method for each data.. -Images with immunohistochemical or HE staining should be shown with scale bars. The quality of images with HE staining (Fig.6) should be improved -The statement in the text “ the tumors of mice transfected with lenti-FoxM1-shRNA were smaller than the control group” does not correspond to that observed in figure 6D. -For data relating to tumor foci and microvascular density (Fig. 6E-G), the number of fields counted per sample, the number of samples and animals evaluated should be indicated -



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The number of patients evaluated with Kaplan-Meier analysis should be indicated.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 59323

Title: Fork head box M1 regulates vascular endothelial growth factor-A expression to promote the angiogenesis and tumor cell growth of gallbladder cancer

Reviewer's code: 02529364

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Senior Lecturer

Reviewer's Country/Territory: Australia

Author's Country/Territory: China

Manuscript submission date: 2020-09-09

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2020-10-26 05:05

Reviewer performed review: 2020-11-17 03:48

Review time: 21 Days and 22 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 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
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

In this article, Wang et al reported their findings of the role of Fork head box M1 (FoxM1) and vascular endothelial growth factor-A (VEGF-A) in primary gallbladder cancer (GBC) using both clinical samples and cell line SGC-996. This article overall was well written. However, revisions are required at several places. Please see my comments below:

1. The article does not have page and line numbers, which makes it very difficult for reviewers to provide comments.
2. Abstract: "Which lacks diagnosis and therapeutic targets". This sentence needs to be revised. How was gallbladder cancer diagnosed if there are no diagnostic targets? Do you mean biomolecular markers?
3. BALB/C nude mice were performed. This needs to be revised. It should be BALB/C nude mice were used to establish the xenograft tumor model.
4. Last paragraph of the introduction "We found that both upregulation and downregulation of FoxM1 are involved in the growth and inhibition of GBC cells, with the possibility of a direct regulatory relationship." This is confusing. Are both upregulation and downregulation of FoxM1 involved in the inhibition of GBC cells? "Tumor cell migration and invasion were also examined to measure the effects of FoxM1 regulation. We aim to explore the mechanism by which FoxM1 regulates VEGF-A in GBC". If this is your aim, please specify in the conclusion what mechanisms have you found?
5. Figure 7: The authors used "high" and "low". What are criteria to define "high" and "low"?