

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 84071

Title: γ -aminobutyric acid B2 receptor: A potential therapeutic target for cholangiocarcinoma in patients with diabetes mellitus

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05575380

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Thailand

Manuscript submission date: 2023-02-23

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-04-01 07:55

Reviewer performed review: 2023-04-01 09:03

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 Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" 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

Dear Editor, thank you so much for inviting me to revise this manuscript about biliary tract cancer. This study addresses a current topic. The manuscript is quite well written and organized. English should be improved. Figures and tables are comprehensive and clear. The introduction explains in a clear and coherent manner the background of this study. We suggest the following modifications:

- Introduction section: although the authors correctly included important papers in this setting, we believe the evolving systemic treatment scenario for BTC should be further discussed and some recently published papers added within the introduction (PMID: 32806956 ; PMID: 36368251; PMID: 33592561; PMID: 33645367), only for a matter of consistency. We think it might be useful to introduce the topic of this interesting study.
- Methods and Statistical Analysis: nothing to add.
- Discussion section: Very interesting and timely discussion. Of note, the authors should expand the Discussion section, including a more personal perspective to reflect on. For example, they could answer the following questions – in order to facilitate the understanding of this complex topic to readers: what potential does this study hold? What are the knowledge gaps and how do researchers tackle them?



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How do you see this area unfolding in the next 5 years? We think it would be extremely interesting for the readers. However, we think the authors should be acknowledged for their work. In fact, they correctly addressed an important topic in renal cell carcinoma, the methods sound good and their discussion is well balanced. One additional little flaw: the authors could better explain the limitations of their work, in the last part of the Discussion. We believe this article is suitable for publication in the journal although major revisions are needed. The main strengths of this paper are that it addresses an interesting and very timely question and provides a clear answer, with some limitations. We suggest a linguistic revision and the addition of some references for a matter of consistency. Moreover, the authors should better clarify some points.

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Title: γ -aminobutyric acid B2 receptor: A potential therapeutic target for cholangiocarcinoma in patients with diabetes mellitus

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05046795

Position: Peer Reviewer

Academic degree: PhD

Professional title: Research Assistant Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Thailand

Manuscript submission date: 2023-02-23

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-04-27 08:15

Reviewer performed review: 2023-04-27 09:40

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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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

I have some concerns about this research: 1. Whether GABBR2 have expression correlation with cyclin D1 or c-Myc in clinical specimen? GABBR2 promote b-cat translocation in CCA cells or tumors? 2. How to choose the concentration of Glc for cells treatment? How about the long term treatment? 3. GAPDH is not an ideal loading control for cancer cells, especially after glucose treatment. 4. They authors should prove that Baclofen treatment can not change the expression of GABBR2. 5. ChIP and other solid evidence should be provided to clarify Baclofen and GABBR2 affect the GSK3/ β -catenin and STAT3 signalling. 6. In vivo experiment, such as xenograft are preferred.

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Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04213605

Position: Peer Reviewer

Academic degree: BSc

Professional title: Teaching Assistant

Reviewer's Country/Territory: Singapore

Author's Country/Territory: Thailand

Manuscript submission date: 2023-02-23

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-04-27 03:10

Reviewer performed review: 2023-05-06 01:40

Review time: 8 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
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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

Overall, it is a decent paper. However, in vivo studies should be included.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Thailand

Manuscript submission date: 2023-02-23

Reviewer chosen by: Jing-Jie Wang

Reviewer accepted review: 2023-06-06 05:00

Reviewer performed review: 2023-06-06 05:01

Review time: 1 Hour

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 checked="" type="radio"/>] Accept (High priority) [<input type="radio"/>] Accept (General priority) [<input type="radio"/>] Minor revision [<input type="radio"/>] Major revision [<input type="radio"/>] Rejection
Peer-reviewer	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

acceptance.