Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 87035

Title: Roles of PI3K Signaling Pathway in Inflammation-Related Cancer: Impact of rs10889677 Variant and Buparlisib in Colitis-Associated Cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05562744
Position: Editorial Board
Academic degree: FACS, MD, PhD
Professional title: Professor, Senior Scientist
Reviewer's Country/Territory: Turkey
Author's Country/Territory: Malaysia

Manuscript submission date: 2023-07-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-07-27 05:15

Reviewer performed review: 2023-07-29 11:00

Review time: 2 Days and 5 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In brief The study aimed to assess the roles of Buparlisib in regulation of PI3K-non-AKT signaling pathway via CAC-induced animal model. CAC model was induced in Balb/c mice with a combination of single azoxymethane injection and three cycles of 2.5% dextran sulfate sodium over the course of ten weeks. CAC-induced mice were subsequently treated orally with PI3K-inhibitor, Buparlisib (30mg/kg/daily) for 14 days. Disease activity index (DAI) was recorded for every two days. The harvested distal colon was stained with haematoxylin and eosin for histological analysis, followed by the immunohistochemistry examination of Ki67 and Cleaved-caspase-3 (CC3; ranging score 0-8) markers. Meanwhile, the proximal colon was processed for quantitative real-time PCR analysis on PDK1 and SGK2 gene. The DAI score was found significantly higher in CAC-induced mice, confirming the successful mice model ($P<0.05$). Buparlisib treatment significantly reduced the mean weight loss in CAC-induced mice (2.0 ± 0.0g) as compared to the untreated CAC-group (2.6 ± 1.8g) ($P<0.05$). Histologically, presence of tumor and moderate inflammation were observed in 50% of CAC-induced mice. Buparlisib-treated CAC-induced mice reduced the proliferative Ki67-positive cells by 5%

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

and had high score of CC3-intensity and -positive cells (6/8). Moreover, Buparlisib treatment also depicted down-regulation trend of PDK1 and SGK2 expression in CAC-induced mice, however, there were not statistically significant as compared to the Buparlisib-untreated group. I believe the mansucript is well wrtten It would benefit from minor language polishing.

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 87035

Title: Roles of PI3K Signaling Pathway in Inflammation-Related Cancer: Impact of rs10889677 Variant and Buparlisib in Colitis-Associated Cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05246699
Position: Peer Reviewer
Academic degree: MSc, PhD
Professional title: Academic Research, Researcher
Reviewer's Country/Territory: Iran
Author's Country/Territory: Malaysia

Manuscript submission date: 2023-07-20
Reviewer chosen by: Geng-Long Liu
Reviewer accepted review: 2023-08-14 07:32
Reviewer performed review: 2023-08-16 05:53
Review time: 1 Day and 22 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript entitled "ROLES OF PI3K-INHIBITOR BUPARLISIB IN COLITIS-ASSOCIATED CANCER MICE MODEL" appears to be interesting, but there are many flaws and concerns on it. Study can be greatly improved if following suggestions were incorporated. 1. The title of the paper is not accurately expressed, and I think it needs to be rewritten. 2. The following reference may increase the reader's comprehension: Sheikholeslami A, Fazaeli H, Kalhor N, Khoshandam M, Eshagh Hoseini SJ, Sheykhhasan M. Use of Mesenchymal Stem Cells in Crohn's Disease and Perianal Fistulas: A Narrative Review. Curr Stem Cell Res Ther. 2023;18(1):76-92. doi: 10.2174/1574888X16666210916145717. PMID: 34530720. 3. It is better to include the results of the inflammation gene expression analysis, including IL-6 and IL-8. 4. In order to make the paper more interesting to read, I suggested that the authors could add one graphical abstract to the manuscript. 5. I suggest including clear limitations of the study in the discussion.

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 87035

Title: Roles of PI3K Signaling Pathway in Inflammation-Related Cancer: Impact of rs10889677 Variant and Buparlisib in Colitis-Associated Cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05260676
Position: Peer Reviewer
Academic degree: FASGE, PhD
Professional title: Surgeon
Reviewer's Country/Territory: China
Author's Country/Territory: Malaysia

Manuscript submission date: 2023-07-20

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-08-20 14:26

Reviewer performed review: 2023-08-23 14:26

Review time: 2 Days and 23 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No creativity or innovation

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [Y] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The PI3K/AKT pathway is involved in the pathogenesis of almost all gastrointestinal tumors, and is not a unique pathogenesis of inflammatory bowel disease-associated bowel cancer. Bupalisib has shown encouraging results in in vivo studies, and the conclusions reached in this study are no different from previous studies. Not much new overall. The mechanism of the down-regulation of PDK1 and SGK2 by Buparlisib needs further study.